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(54) Title: METHODS AND COMPOSITIONS FOR DIAGNOSING AND MONITORING TRANSPLANT REJECTION

(57) Abstract: Methods of diagnosing or monitoring transplant rejection, particularly cardiac transplant rejection, in a patient by
detecting the expression level of one or more genes in a patient, are described. Diagnostic oligonucleotides for diagnosing or moni-
toring transplant rejection, particularly cardiac transplant rejection and kits or systems containing the same are also described.

METHODS AND COMPOSITIONS FOR DIAGNOSING
AND MONITORING TRANSPLANT REJECTION

Related Applications

This application claims priority to U.S. Application No. 10/131,831, filed April 24, 2002, and U.S. Application No. 10/325,899, filed December 20, 2002.

Field of the Invention

This invention is in the field of expression profiling following organ transplantation.

Background of the Invention

Many of the current shortcomings in diagnosis, prognosis, risk stratification and treatment of disease can be approached through the identification of the molecular mechanisms underlying a disease and through the discovery of nucleotide sequences (or sets of nucleotide sequences) whose expression patterns predict the occurrence or progression of disease states, or predict a patient's response to a particular therapeutic intervention. In particular, identification of nucleotide sequences and sets of nucleotide sequences with such predictive value from cells and tissues that are readily accessible would be extremely valuable. For example, peripheral blood is attainable from all patients and can easily be obtained at multiple time points at low cost. This is a desirable contrast to most other cell and tissue types, which are less readily accessible, or accessible only through invasive and aversive procedures. In addition, the various cell types present in circulating blood are ideal for expression profiling experiments as the many cell types in the blood specimen can be easily separated if desired prior to analysis of gene expression. While blood provides a very attractive substrate for the study of diseases using expression profiling techniques, and for the development of diagnostic technologies and the identification of therapeutic targets, the value of expression profiling in blood samples rests on the degree to which changes in gene expression in these cell types are associated with a predisposition to, and pathogenesis and progression of a disease.

Hematopoiesis is the development and maturation of all cell types of the blood. These include erythrocytes, platelets and leukocytes. Leukocytes are further subdivided into granulocytes (neutrophils, eosinophils, basophils) and mononuclear cells (monocytes, lymphocytes). These cells develop and mature from precursor cells to replenish the circulating pool and to respond to insults and challenges to the system. This occurs in the bone marrow, spleen, thymus, liver, lymph nodes, mucosal associated lymphoid tissue (MALT) and peripheral blood.

Precursor cells differentiate into immature forms of each lineage and these immature cells develop further into mature cells. This process occurs under the influence and direction of hematopoietic growth factors. When hematopoiesis is stimulated, there is an increase in the number of immature cells in the peripheral blood and in some cases, precursor cells are found at increased frequency. For example, CD34+ cells (hematopoietic stem cells) may increase in frequency in the peripheral blood with an insult to the immune system. For neutrophils, "band" forms are increased, for erythrocytes, reticulocytes or nucleated red cells are seen. Lymphocytes are preceeded by lymphoblasts (immature lymphocytes).

It may be an important clinical goal to measure the rate of production of blood cells of a variety of lineages. Hematological disorders involving over or under production of various blood cells

may be treated pharmacologically. For example, anemia (low red blood cells) may be treated with erythropoietin (a hematopoietic growth factor) and response to this therapy can be assessed by measuring RBC production rates. Low neutrophils counts can be treated by administration of G-CSF and this therapy may be monitored by measuring neutrophil production rates. Alternatively, the diagnosis of blood cell disorders is greatly facilitated by determination of lineage specific production rates. For example, anemia (low RBCs) may be caused by decreased cellular production or increased destruction of cells. In the latter case, the rate of cellular production will be increased rather than decreased and the therapeutic implications are very different. Further discussion of the clinical uses of measures of blood cell production rates is given in below.

Assessment of blood cell production rates may be useful for diagnosis and management of non-hematological disorders. In particular, acute allograft rejection diagnosis and monitoring may benefit from such an approach. Current diagnosis and monitoring of acute allograft rejection is achieved through invasive allograft biopsy and assessment of the biopsy histology. This approach is sub-optimal because of expense of the procedure, cost, pain and discomfort of the patient, the need for trained physician operators, the risk of complications of the procedure, the lack of insight into the functioning of the immune system and variability of pathological assessment. In addition, biopsy can diagnose acute allograft rejection only after significant cellular infiltration into the allograft has occurred. At this point, the process has already caused damage to the allograft. For all these reasons, a simple blood test that can diagnose and monitor acute rejection at an earlier stage in the process is needed. Allograft rejection depends on the presence of functioning cells of the immune system. In addition, the process of rejection may cause activation of hematopoiesis. Finally, effective immunosuppressive therapy to treat or prevent acute rejection may suppress hematopoiesis. For these reasons, assessment of hematopoietic cellular production rates may be useful in the diagnosis and monitoring of acute rejection.

Current techniques for measuring cellular development and production rates are inadequate. The most common approach is to measure the number of mature cells of a lineage of interest over time. For example, if a patient is being treated for anemia (low red blood cell counts), then the physician will order a blood cell count to assess the number of red blood cells (RBCs) in circulation. For this to be effective, the physician must measure the cell count over time and may have to wait 2-4 weeks before being able to assess response to therapy. The same limitation is true for assessment of any cell lineage in the blood.

An alternative approach is to count the number of immature cells in the peripheral blood by counting them under the microscope. This may allow a more rapid assessment of cellular production rates, but is limited by the need for assessment by a skilled hematologist, observer variability and the inability to distinguish all precursor cells on the basis of morphology alone.

Bone marrow biopsy is the gold standard for assessment of cellular production rates. In addition to the limitations of the need for skilled physicians, reader variability and the lack of sensitivity of morphology alone, the technique is also limited by the expense, discomfort to the patient and need for a prolonged visit to a medical center. Thus there is a need for a reliable, rapid means for measuring the rate of hematopoeisis in a patient.

In addition to the relationship between hematopoiesis and variety of disease processes, there is an extensive literature supporting the role of leukocytes, e.g., T-and B-lymphocytes, monocytes and granulocytes, including neutrophils, in a wide range of disease processes, including such broad classes as cardiovascular diseases, inflammatory, autoimmune and rheumatic diseases, infectious diseases, transplant rejection, cancer and malignancy, and endocrine diseases. For example, among cardiovascular diseases, such commonly occurring diseases as atherosclerosis, restenosis, transplant vasculopathy and acute coronary syndromes all demonstrate significant T cell involvement (Smith-Norowitz et al. (1999) Clin Immunol 93:168-175; Jude et al. (1994) Circulation 90:1662-8; Belch et al. (1997) Circulation 95:2027-31). These diseases are now recognized as manifestations of chronic inflammatory disorders resulting from an ongoing response to an injury process in the arterial tree (Ross et al. (1999) Ann Thorac Surg 67:1428-33). Differential expression of lymphocyte, monocyte and neutrophil genes and their products has been demonstrated clearly in the literature. Particularly interesting are examples of differential expression in circulating cells of the immune system that demonstrate specificity for a particular disease, such as arteriosclerosis, as opposed to a generalized association with other inflammatory diseases, or for example, with unstable angina rather than quiescent coronary disease.

A number of individual genes, e.g., CD11b/CD18 (Kassirer et al. (1999) Am Heart J 138:555-9); leukocyte elastase (Amaro et al. (1995) Eur Heart J 16:615-22; and CD40L (Aukrust et al. (1999) Circulation 100:614-20) demonstrate some degree of sensitivity and specificity as markers of various vascular diseases. In addition, the identification of differentially expressed target and fingerprint genes isolated from purified populations of monocytes manipulated in various in vitro paradigms has been proposed for the diagnosis and monitoring of a range of cardiovascular diseases, see, e.g., US Patents Numbers 6,048,709; 6,087,477; 6,099,823; and 6,124,433 "COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF CARDIOVASCULAR DISEASE" to Falb (see also, WO 97/30065). Lockhart, in US Patent Number 6,033,860 "EXPRESSION PROFILES IN ADULT AND FETAL ORGANS" proposes the use of expression profiles for a subset of identified genes in the identification of tissue samples, and the monitoring of drug effects.

The accuracy of technologies based on expression profiling for the diagnosis, prognosis, and monitoring of disease would be dramatically increased if numerous differentially expressed nucleotide sequences, each with a measure of specificity for a disease in question, could be identified and assayed in a concerted manner. PCT application WO 02/057414 "LEUKOCYTE EXPRESSION PROFILING" to Wohlgemuth identifies one such set of differentially expressed nucleotides.

In order to achieve this improved accuracy, the sets of nucleotide sequences once identified need to be validated to identify those differentially expressed nucleotides within a given set that are most useful for diagnosis, prognosis, and monitoring of disease. The present invention addresses these and other needs, and applies to transplant rejection and detection of the rate of hematopoeisis for which differential regulation of genes, or other nucleotide sequences, of peripheral blood can be demonstrated.

Summary of the Invention

In order to meet these needs, the present invention is thus directed to a system for detecting differential gene expression. In one format, method are provided for assessing the immune status of an individual by detecting the expression level of one or more genes expressed at different levels depending upon the rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in the individual. The one or more genes may include a nucleotide selected from a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,

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NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID
NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID
NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. The expression level may be detected by measuring
the RNA level expressed by the one or more genes. In one variation, the RNA level is detected by
PCR. In another variation, the RNA level is detected by hybridization. The expression level may also
be detected by measuring one or more proteins expressed by the one or more genes.

The present invention is further directed to methods of diagnosing or monitoring transplant
rejection in an individual by detecting a rate of hematopoiesis. The detection may be applied directly
to the individual, or to a sample isolated from the individual. Detection may be accomplished by RNA
profiling assay, immunoassay, fluorescent activated cell sorting, protein assay, peripheral blood
cytology assay, MRI imaging, bone marrow aspiration, and/or nuclear imaging. In one variation, the
RNA profile assay is a PCR based assay. In another variation, the RNA profile assay is a hybridization
based assay. The RNA profile assay may further include detecting the expression level of one or more
genes in the individual where the one or more genes include a nucleotide sequence selected from SEQ
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NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID

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NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID
NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID
NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID
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NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID
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NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID
NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID
NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID
NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID
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NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID
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NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID
NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID
NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID
NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID
NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. Transplant
rejection may include one or more of heart transplant rejection, kidney transplant rejection, liver
transplant rejection, pancreas transplant rejection, pancreatic islet transplant rejection, lung transplant
rejection, bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and
mechanical organ replacement rejection.

In another aspect, the invention is directed to a method of diagnosing or monitoring transplant
rejection in a patient by detecting the expression level of one or more genes in the patient to diagnose
or monitor transplant rejection in the patient, wherein the one or more genes include a nucleotide
sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,
SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ
ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID
NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID
NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID
NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID
NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID
NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID
NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID

NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ

ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317,
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NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ
ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID
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NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID
NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID
NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID
NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID
NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID
NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID
NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID
NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID
NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. In one variation, the invention is further directed to
detecting the expression level of one or more additional genes in the patient to diagnose or monitor
transplant rejection in the patient, wherein the one or more additional genes include a nucleotide
sequence selected from SEQ ID NO:8, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID
NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:97, SEQ ID
NO:99, SEQ ID NO:100, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145,
SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID
NO:15.

In a further variation, the invention is directed to a method of diagnosing or monitoring
cardiac transplant rejection in a patient by detecting the expression level of one or more genes in the

patient to diagnose or monitor cardiac transplant rejection in the patient wherein the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ

ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332. In one variation, the method includes detecting the expression level of one or more additional genes in the patient to diagnose or monitor cardiac transplant rejection in the patient, wherein the one or more additional genes include a nucleotide sequence selected from SEQ ID NO:8, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:97, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151.

The invention is also directed to a method of diagnosing or monitoring kidney transplant rejection in a patient by detecting the expression level of one or more genes in the patient to diagnose or monitor kidney transplant rejection in the patient wherein the one or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:78, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID

NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID

NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729. In one variation, the method further includes detecting the expression level of one or more additional genes in the patient to diagnose or monitor kidney transplant rejection in a patient, wherein the one or more additional genes includes a nucleotide sequence selected from SEQ ID NO: 75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151.

In another aspect, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least two of the genes. In another variation, methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least ten of the genes. In a further variation, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of at least one hundred of the genes. In still a further variation, the methods of diagnosing or monitoring transplant rejection include detecting the expression level of all the listed genes.

In another variation, transplant rejection may be selected from heart transplant rejection, kidney transplant rejection, liver transplant rejection, pancreas transplant rejection, pancreatic islet

transplant rejection, lung transplant rejection, bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and mechanical organ replacement rejection.

In another aspect, the methods of detecting transplant rejection include detecting the expression level by measuring the RNA level expressed by one or more genes. The method may further including isolating RNA from the patient prior to detecting the RNA level expressed by the one or more genes.

In one variation, the RNA level is detected by PCR. In a still further variation, the PCR uses primers consisting of nucleotide sequences selected from the group consisting of SEQ ID NO:665, SEQ ID NO:666, SEQ ID NO:667, SEQ ID NO:668, SEQ ID NO:669, SEQ ID NO:670, SEQ ID NO:671, SEQ ID NO:672, SEQ ID NO:673, SEQ ID NO:674, SEQ ID NO:675, SEQ ID NO:676, SEQ ID NO:677, SEQ ID NO:678, SEQ ID NO:679, SEQ ID NO:680, SEQ ID NO:681, SEQ ID NO:682, SEQ ID NO:683, SEQ ID NO:684, SEQ ID NO:685, SEQ ID NO:686, SEQ ID NO:687, SEQ ID NO:688, SEQ ID NO:689, SEQ ID NO:690, SEQ ID NO:691, SEQ ID NO:692, SEQ ID NO:693, SEQ ID NO:694, SEQ ID NO:695, SEQ ID NO:696, SEQ ID NO:697, SEQ ID NO:698, SEQ ID NO:699, SEQ ID NO:700, SEQ ID NO:701, SEQ ID NO:702, SEQ ID NO:703, SEQ ID NO:704, SEQ ID NO:705, SEQ ID NO:706, SEQ ID NO:707, SEQ ID NO:708, SEQ ID NO:709, SEQ ID NO:710, SEQ ID NO:711, SEQ ID NO:712, SEQ ID NO:713, SEQ ID NO:714, SEQ ID NO:715, SEQ ID NO:716, SEQ ID NO:717, SEQ ID NO:718, SEQ ID NO:719, SEQ ID NO:720, SEQ ID NO:721, SEQ ID NO:722, SEQ ID NO:723, SEQ ID NO:724, SEQ ID NO:725, SEQ ID NO:726, SEQ ID NO:727, SEQ ID NO:728, SEQ ID NO:729, SEQ ID NO:730, SEQ ID NO:731, SEQ ID NO:732, SEQ ID NO:733, SEQ ID NO:734, SEQ ID NO:735, SEQ ID NO:736, SEQ ID NO:737, SEQ ID NO:738, SEQ ID NO:739, SEQ ID NO:740, SEQ ID NO:741, SEQ ID NO:742, SEQ ID NO:743, SEQ ID NO:744, SEQ ID NO:745, SEQ ID NO:746, SEQ ID NO:747, SEQ ID NO:748, SEQ ID NO:749, SEQ ID NO:750, SEQ ID NO:751, SEQ ID NO:752, SEQ ID NO:753, SEQ ID NO:754, SEQ ID NO:755, SEQ ID NO:756, SEQ ID NO:757, SEQ ID NO:758, SEQ ID NO:759, SEQ ID NO:760, SEQ ID NO:761, SEQ ID NO:762, SEQ ID NO:763, SEQ ID NO:764, SEQ ID NO:765, SEQ ID NO:766, SEQ ID NO:767, SEQ ID NO:768, SEQ ID NO:769, SEQ ID NO:770, SEQ ID NO:771, SEQ ID NO:772, SEQ ID NO:773, SEQ ID NO:774, SEQ ID NO:775, SEQ ID NO:776, SEQ ID NO:777, SEQ ID NO:778, SEQ ID NO:779, SEQ ID NO:780, SEQ ID NO:781, SEQ ID NO:782, SEQ ID NO:783, SEQ ID NO:784, SEQ ID NO:785, SEQ ID NO:786, SEQ ID NO:787, SEQ ID NO:788, SEQ ID NO:789, SEQ ID NO:790, SEQ ID NO:791, SEQ ID NO:792, SEQ ID NO:793, SEQ ID NO:794, SEQ ID NO:795, SEQ ID NO:796, SEQ ID NO:797, SEQ ID NO:798, SEQ ID NO:799, SEQ ID NO:800, SEQ ID NO:801, SEQ ID NO:802, SEQ ID NO:803, SEQ ID NO:804, SEQ ID NO:805, SEQ ID NO:806, SEQ ID NO:807, SEQ ID NO:808, SEQ ID NO:809, SEQ ID NO:810, SEQ ID NO:811, SEQ ID NO:812, SEQ ID NO:813, SEQ ID NO:814, SEQ ID NO:815, SEQ ID NO:816, SEQ ID NO:817, SEQ ID NO:818, SEQ ID NO:819, SEQ ID NO:820, SEQ ID NO:821, SEQ ID NO:822, SEQ ID NO:823, SEQ ID NO:824, SEQ ID NO:825, SEQ ID NO:826, SEQ ID NO:827, SEQ ID NO:828, SEQ ID NO:829, SEQ ID NO:830, SEQ ID NO:831, SEQ ID NO:832, SEQ ID NO:833, SEQ ID NO:834, SEQ ID NO:835, SEQ ID NO:836, SEQ ID NO:837, SEQ ID NO:838, SEQ ID NO:839, SEQ ID NO:840, SEQ ID NO:841, SEQ ID NO:842, SEQ ID NO:843, SEQ ID NO:844, SEQ ID NO:845, SEQ ID NO:846, SEQ

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NO:2144, SEQ ID NO:2145, SEQ ID NO:2146, SEQ ID NO:2147, SEQ ID NO:2148, SEQ ID
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consisting of nucleotide sequences selected from the group consisting of SEQ ID NO:1327, SEQ ID
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NO:2393, SEQ ID NO:2394, SEQ ID NO:2395, SEQ ID NO:2396, SEQ ID NO:2397, SEQ ID
NO:2398, SEQ ID NO:2399. The RNA level may be detected by hybridization to the probes. In a
further variation, the RNA level is detected by hybridization to an oligonucleotide. Examples of
oligonucleotide include oligonucleotides having a nucleotide sequence selected from SEQ ID NO:2,
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oligonucleotide has a nucleotide sequence consisting of SEQ ID NO: 107. The oligonucleotide may be DNA, RNA, cDNA, PNA, genomic DNA, or synthetic oligonucleotides.

In another aspect, the methods of detecting transplant rejection include detecting the expression level by measuring one or more proteins expressed by the one or more genes. In one variation, the one or more proteins include an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID NO:2533, SEQ ID NO:2534, SEQ ID NO:2535, SEQ ID NO:2536, SEQ ID NO:2537, SEQ ID NO:2538, SEQ ID NO:2539, SEQ ID NO:2540, SEQ ID NO:2541, SEQ ID NO:2542, SEQ ID NO:2543, SEQ ID NO:2544, SEQ ID NO:2545, SEQ ID NO:2546, SEQ ID NO:2547, SEQ ID NO:2548, SEQ ID NO:2549, SEQ ID NO:2550, SEQ ID NO:2551, SEQ ID NO:2552, SEQ ID NO:2553, SEQ ID NO:2554, SEQ ID NO:2555, SEQ ID NO:2556, SEQ ID NO:2557, SEQ ID NO:2558, SEQ ID NO:2559, SEQ ID NO:2560, SEQ ID NO:2561, SEQ ID NO:2562, SEQ ID NO:2563, SEQ ID NO:2564, SEQ ID NO:2565, SEQ ID NO:2566, SEQ ID NO:2567, SEQ ID NO:2568, SEQ ID NO:2569, SEQ ID NO:2570, SEQ ID NO:2571, SEQ ID NO:2572, SEQ ID NO:2573, SEQ ID NO:2574, SEQ ID NO:2575, SEQ ID NO:2576, SEQ ID NO:2577, SEQ ID NO:2578, SEQ ID NO:2579, SEQ ID NO:2580, SEQ ID NO:2581, SEQ ID NO:2582, SEQ ID NO:2583, SEQ ID NO:2584, SEQ ID NO:2585, SEQ ID NO:2586, SEQ ID NO:2587, SEQ ID NO:2588, SEQ ID NO:2589, SEQ ID NO:2590, SEQ ID NO:2591, SEQ ID NO:2592, SEQ ID NO:2593, SEQ ID NO:2594, SEQ ID NO:2595, SEQ ID NO:2596, SEQ ID NO:2597, SEQ ID NO:2598, SEQ ID

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NO:2997, SEQ ID NO:2998, SEQ ID NO:2999, SEQ ID NO:3000, SEQ ID NO:3001, SEQ ID
NO:3002, SEQ ID NO:3003, SEQ ID NO:3004, SEQ ID NO:3005, SEQ ID NO:3006, SEQ ID
NO:3007, SEQ ID NO:3008, SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID
NO:3012, SEQ ID NO:3013, SEQ ID NO:3014, SEQ ID NO:3015. In a further variation, the the
method includes detecting one or more additional proteins expressed by SEQ ID NO:2406, SEQ ID
NO:2431, SEQ ID NO:2471, SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID NO:2474, SEQ ID
NO:2475, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2484, SEQ ID NO:2487, SEQ ID
NO:2489, SEQ ID NO:2490, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID
NO:2501, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ ID
NO:2526, SEQ ID NO:2527. In still another variation, one or more proteins may be selected from
SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID
NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID
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In another aspect, the method of diagnosing or monitoring cardiac transplant rejection in a patient includes detecting the expression level of one or more genes in the patient to diagnose or monitor cardiac transplant rejection in the patient by measuring one or more proteins expressed by the one or more genes. The one or more proteins may include an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2471, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2484, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID NO:2501, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID

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NO:2618, SEQ ID NO:2619, SEQ ID NO:2620, SEQ ID NO:2621, SEQ ID NO:2622, SEQ ID
NO:2623, SEQ ID NO:2624, SEQ ID NO:2625, SEQ ID NO:2626. Alternatively, the expression level
of the one or more genes may be detected by measuring one or more proteins expressed by one or more
genes, and one or more proteins expressed by one or more additional genes. In one variation, the one
or more proteins expressed by the one or more genes include an amino acid sequence selected from
SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID
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NO:2593, SEQ ID NO:2594, SEQ ID NO:2595, SEQ ID NO:2596, SEQ ID NO:2597, SEQ ID

NO:2598, SEQ ID NO:2599, SEQ ID NO:2600, SEQ ID NO:2601, SEQ ID NO:2602, SEQ ID

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NO:2613, SEQ ID NO:2614, SEQ ID NO:2615, SEQ ID NO:2616, SEQ ID NO:2617, SEQ ID

NO:2618, SEQ ID NO:2619, SEQ ID NO:2620, SEQ ID NO:2621, SEQ ID NO:2622, SEQ ID

NO:2623, SEQ ID NO:2624, SEQ ID NO:2625, SEQ ID NO:2626, and the one or more protein

expressed by the one or more additional genes include an amino acid sequence selected from the group

consisting of SEQ ID NO:2406, SEQ ID NO:2431, SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID

NO:2474, SEQ ID NO:2475, SEQ ID NO:2487, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID

NO:2524, SEQ ID NO:2525, SEQ ID NO:2526, SEQ ID NO:2527.

In another aspect, the method of diagnosing or monitoring kidney transplant rejection in a

patient includes detecting the expression level of one or more genes in the patient to diagnose or

monitor kidney transplant rejection in the patient by measuring one or more proteins encoded by the

one or more genes. In one variation, the one or more proteins include an amino acid sequence selected

from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404,

SEQ ID NO:2405, SEQ ID NO:2406, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID

NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID

NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID

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NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID

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NO:3003, SEQ ID NO:3004, SEQ ID NO:3005, SEQ ID NO:3006, SEQ ID NO:3007, SEQ ID
NO:3008, SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID
NO:3013, SEQ ID NO:3014, SEQ ID NO:3015. In another variation, the method includes detectin g
the expression level of one or more additional genes by measuring one or more proteins expressed by
the one or more additional genes. The one or more proteins expressed by the one or more genes
comprises an amino acid sequence selected from SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID
NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2406, SEQ ID
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NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID NO:3013, SEQ ID NO:3014, SEQ ID
NO:3015, and the one or more proteins expressed by the one or more additional genes may include an
amino acid sequence selected from SEQ ID NO:2431, SEQ ID NO:2471, SEQ ID NO:2472, SEQ ID
NO:2473, SEQ ID NO:2475, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2484, SEQ ID
NO:2489, SEQ ID NO:2490, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID
NO:2501, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ ID
NO:2526, SEQ ID NO:2527.

Protein detection may be accomplished by measuring serum. In another variation, the protein is a cell surface protein. In a further variation, the measuring includes using a fluorescent activated cell sorter.

In another aspect, the invention is directed to a substantially purified oligonucleotide having the nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ

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NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID
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having at least 90% sequence identity to an oligonucleotide having the nucleotide sequence selected
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NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID
NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID
NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID
NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID
NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID
NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID
NO:2729 and/or SEQ ID NO:333-664. In a further aspect, the invention is directed to a substantially
purified oligonucleotide that hybridizes at high stringency to an oligonucleotide having the nucleotide
sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6,
SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ
ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID
NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID
NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID
NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID
NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID
NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID
NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID
NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID
NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID
NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID
NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID
NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID
NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID
NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID
NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID
NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ
ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114,
SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID
NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ
ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131,
SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ
ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,

SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID

NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729 or SEQ ID NOS:333-664. The sequences may be used as diagnostic oligonucleotides for transplant rejection and/or cardiac transplant rejection. The oligonucleotide may have nucleotide sequence including DNA, cDNA, PNA, genomic DNA, or synthetic oligonucleotides.

In another aspect, the invention is directed to a method of diagnosing or monitoring transplant rejection in a patient wherein the expression level of one or more genes in a patient's bodily fluid is detected. In a further variation, the bodily fluid is peripheral blood.

In another aspect, the invention is directed to a method of diagnosing or monitoring transplant rejection in a patient, comprising detecting the expression level of four or more genes in the patient to diagnose or monitor transplant rejection in the patient wherein the four or more genes include a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID

NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID

NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729.

In another aspect, the invention is directed to a method of diagnosing or monitoring kidney transplant rejection in a patient by detecting one or more proteins in a bodily fluid of the patient to diagnose or monitor transplant rejection in the patient wherein the one or more proteins have a protein sequence selected from SEQ ID NO:76, SEQ ID NO:2663, SEQ ID NO:98, SEQ ID NO:2696, SEQ ID NO:2736, SEQ ID NO:2751, SEQ ID NO:2631, SEQ ID NO:2675, SEQ ID NO:2700, and SEQ ID NO:2693.

In a further aspect, the invention is also directed to a system for detecting gene expression in body fluid including at least two isolated polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the gene includes a nucleotide sequence selected from SEQ ID NO:2,

SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262,

SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729 and the gene is differentially expressed in body fluid in an individual rejecting a transplanted

organ compared to the expression of the gene in leukocytes in an individual not rejecting a transplanted organ.

In another aspect, the invention is directed to a system for detecting gene expression in body fluid including at least two isolated polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the gene includes a nucleotide sequence selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ

ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID

NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID

NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID

NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID

NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID

NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID

NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID

NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID

NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729 and the gene

expression is related to the rate of hematopoiesis or the distribution of hematopoeitic cells along their

maturation pathway.

The invention is also directed to methods of diagnosing or monitoring transplant rejection in a

patient by detecting the expression level of one or more genes including a nucleotide sequence selected

from SEQ ID NOS: 3016-3117. SEQ ID NOS:3108-3117 are useful in detecting CMV infection.

Brief Description of the Sequence Listing

SEQ ID's 1-332 are 50mer oligonucleotides corresponding to gene expression markers for diagnosis
and monitoring of allograft rejection and other disorders.

SEQ ID's 333-664 are Reference mRNA sequences for genes identified by probes 1-332.

SEQ ID's 665-995 are a first set of Left PCR primers for genes 1-332.

SEQ ID's 996-1326 are a first set of Right PCR primers for genes 1-332.

SEQ ID's 1327-1657 are Taqman probes for the first set PCR primers for genes 1-332.

SEQ ID's 1658-1903 are a second alternative set of left PCR primers for selected genes 1-332

SEQ ID's 1904-2151 are a second alternative set of right PCR primers for selected genes 1-332

SEQ ID's 2152-2399 are Taqman probes for the second alternative set of PCR primers for selected
genes 1-332.

SEQ ID's 2400-2626 are Proteins encoded by mRNA's from genes identified in 1-332.

SEQ ID's 2627-2795 are 50mer oligonucleotide array probes used to identify genes in Figure 7 and
Tables 6 and 8.

SEQ ID's 2796-2924 are reference mRNA sequences for genes in Table 8 which show altered
expression in renal transplantation and rejection.

SEQ ID's 2925-3015 are proteins coded by genes which show altered expression in Table 8.

SEQ ID's 3016-3081 are 50mer oligonucleotide array probes and used to identify genes in the
Examples.

SEQ ID's 3082-3107 are genes and primers discussed in the Examples.

SEQ ID's 3108-3117 are mRNAs from human genes in which regulation is altered upon CMV
infection.

Brief Description of the Figures

Figure 1: Figure 1 is a schematic flow chart illustrating a schematic instruction set for characterization
of the nucleotide sequence and/or the predicted protein sequence of novel nucleotide sequences.

Figure 2: Figure 2 depicts the components of an automated RNA preparation machine.

Figure 3 shows the results of six hybridizations on a mini array graphed (n=6 for each column). The error bars are the SEM. This experiment shows that the average signal from AP prepared RNA is 47% of the average signal from GS prepared RNA for both Cy3 and Cy5.

Figure 4 shows the average background subtracted signal for each of nine leukocyte-specific genes on a mini array. This average is for 3-6 of the above-described hybridizations for each gene. The error bars are the SEM.

Figure 5 shows the ratio of Cy3 to Cy5 signal for a number of genes. After normalization, this ratio corrects for variability among hybridizations and allows comparison between experiments done at different times. The ratio is calculated as the Cy3 background subtracted signal divided by the Cy5 background subtracted signal. Each bar is the average for 3-6 hybridizations. The error bars are SEM.

Figure 6 shows data median Cy3 background subtracted signals for control RNAs using mini arrays.

Figure 7: Cardiac Allograft rejection diagnostic genes.

A. Example of rejection and no-rejection samples expression data for 5 marker genes. For each sample, the associated rejection grades are shown as are the expression ratios for 5 differentially expressed genes. The genes are identified by the SEQ ID number for the oligonucleotide. The average fold difference between grade 0 and grade 3A samples is calculated at the bottom.

B. CART classification model. Decision tree for a 3 gene classification model for diagnosis of cardiac rejection. In the first step, expression of gene 223 is used to divide the patients to 2 branches. The remaining samples in each branch are then further divided by one remaining gene. The samples are classified as either rejection or no rejection. 1 no rejection sample is misclassified as a rejection sample.

C. Surrogates for the CART classification model. For each of the 3 splitter genes in the CART rejection model described in the example, 5 top surrogate genes are listed that were identified by the CART algorithm.

Figure 8: Validation of differential expression of a gene discovered using microarrays using real-time PCR

Figure 8A. The Ct for each patient sample on multiple assays is shown along with the Ct in the R50 control RNA. Triangles represent –RT (reverse transcriptase) controls.

Figure 8B. The fold difference between the expression of Granzyme B and an Actin reference is shown for 3 samples from patients with and without CMV disease.

Figure 9: Endpoint testing of PCR primers

Electrophoresis and microfluidics are used to assess the product of gene specific PCR primers.

β-GUS gel image. Lane 3 is the image for primers F178 and R242. Lanes 2 and 1 correspond to the no-template control and –RT control, respectively.

The electropherogram of β-GUS primers F178 and R242, a graphical representation of Lane 3 from the gel image.

β-Actin gel image. Lane 3 is the image for primers F75 and R178. Lanes 2 and 1 correspond to the no-template control and –RT control, respectively.

The electropherogram of β-Actin primers F75 and R178, a graphical representation of Lave 3 from the gel image.

Figure 10: PCR Primer efficiency testing. A standard curve of Ct versus log of the starting RNA amount is shown for 2 genes.

Figure 11: Real-time PCR control gene analysis

11 candidate control genes were tested using real-time PCR on 6 whole blood samples (PAX) paired with 6 mononuclear samples (CPT) from the same patient. Each sample was tested twice. For each gene, the variability of the gene across the samples is shown on the vertical axis (top graph). The average Ct value for each gene is also shown (bottom graph). 2ug RNA was used for PAX samples and 0.5 ug total RNA was used for the mononuclear samples (CPT).

Figure 12: Rejection marker discovery by co-expression with established marker

Microarrays were used to measure expression of genes SEQ ID 85 and 302 in samples derived from 240 transplant recipients. For each sample, the expression measurement for 85 is plotted against 302.

Figure 13: ROC (receiver operator characteristics) curve for a 3-gene PCR assay for diagnosis of rejection (see example 17). The Sensitivity and False Positive Rate for each test cutoff is shown.

Brief Description of the Tables

Table 1: Table 1 lists diseases or conditions amenable to study by leukocyte profiling.

Table 2: Transplant Markers

A. Transplant Genes: Genes useful for monitoring of allograft rejection are listed in this here. The gene symbol and name are given. SEQ ID 50mer is the sequence ID of a 50mer oligonucleotide that is specific for the gene. The NCBI Unigene number (HS) from (Build 160, 16 Feb 2003) is given as is an accession number (ACC) from (Genbank Release 135, 15 April 2003) for an RNA or cDNA is Genbank that corresponds to the gene. The sequence identified by the ACC number is in the sequence listing (SEQ ID RNA/cDNA).

B. Microarray Data: SEQ ID 50mer, Gene, Gene Name, ACC and SEQ ID RNA/cDNA are given for each gene as in A (above). Each identified gene has a Non-Parametric Score and Median Rank in NR given from the non-parametric analysis of the data. The genes are ranked from highest to lowest scoring. Down Regulated genes are noted with a 1 in this column.

C. PCR Primers: Primers and probes for real-time PCR assays for each gene are given along with their SEQ ID #s. Each gene has 1 or 2 sets of a forward and reverse PCR primer and a hybridization probe for detection in TaqMan or similar assays.

D. PCR Data: Real-time PCR data was generated on a set of transplant samples using sybr green technology as described in the text. For each gene the number of samples (n) used in the analysis is given. An odds ratio and the p-values for a Fisher test and t-test are given for the comparison of acute rejection samples is given (see text).

E. Transplant proteins: For each gene, the corresponding protein in the RefSeq data base (Genbank Release 135, 18 April 2003) is given (RefSeq Peptide Accession #) along the the SEQ ID for that protein for the sequence listing.

Table 3: Viral gene for arrays. Viral genomes were used to design oligonucleotides for the microarrays. The accession numbers for the viral genomes used are given, along with the gene name and location of the region used for oligonucleotide design.

Table 4. Dependent variables for discovery of gene expression markers of cardiac allograft rejection. A stable Grade 0 is a Grade 0 biopsy in a patient who does not experience rejection with the subsequent biopsy. HG or highest grade means that the higher of the biopsy grades from the centralized and local pathologists was used for a definition of the dependent variable.

Table 5: Real-time PCR assay reporter and quencher dyes. Various combinations of reporter and quencher dyes are useful for real-time PCR assays. Reporter and quencher dyes work optimally in specific combinations defined by their spectra. For each reporter, appropriate choices for quencher dyes are given.

Table 6: Rejection marker PCR assay results

Results of real-time PCR assays are listed for the comparison of rejection samples to no rejection samples. The fold change is given for expression of each gene in rejection/no rejection samples. The p-value for the t-test comparing the rejection and no rejection classes is given.

Table 7: Summary results of array rejection significance analysis. Summary results are given for correlation analysis of leukocyte gene expression to acute rejection using significance analysis for microarrays (SAM). Five analyses are described. The ISHLT grades used to define the rejection and no rejection classes are given. In each case the highest grade from three pathology reading was taken for analysis. All samples are used for two analyses. The other analyses reduce redundancy of patients used in the analysis by using only one sample per patient ("Non-redundant") or using only one sample per patient within a given class ("Non-redundant within class"). The number of samples used in the analysis is given and the lowest false detection rate (FDR) achieved is noted.

Table 8: Renal tissue rejection array significance analysis. Genes are listed that were identified as upregulated using microarrays on renal tissue with acute rejection versus controls. Significance analysis for microarrays (SAM) was used to determine the false detection rate for each gene (FDR). Genes with known expression in leukocytes are noted in the table.

Table 9: Rejection marker sequence analysis. For 63 of the allograft rejection markers listed in Table 2, an analysis of the gene sequence was done. The genes and proteins are identified by accession numbers. The cellular localization of each gene is described as either secreted, nuclear, mitochondrial, cytoplasmic or cellular membrane. The function of the gene is also described.

Table 10: Gene expression markers for immature cells of a variety of lineages are given in Table 10 by way of example

Table 11: Changes in the rate of hematopoiesis have been correlated to a number of disease states and other pathologies. Examples of such conditions are listed in Table 11.

Table 12: This table lists the oligonucleotides and associated genes identified as having value for the diagnosis and monitoring of CMV infection. The first column gives the SEQ ID that corresponds to the oligonuclotide in the sequence listing. The unigene number, genebank accession and GI number are also given for each sequence when known. The name of the gene associated with the accession number is noted. The strand is noted as –1 or 1, meaning that the probe was designed from the complement of the sequence (-1) or directly from the sequence (1). Next, the nucleotide sequence of each probe is also given. For each gene, the false detection rate (FDR) from the significance analsysis described in

example 7 is given if applicable. WBC is the white blood cell count. WPT is the number of weeks past transplant.

Detailed Description of the Invention

Definitions

Unless defined otherwise, all scientific and technical terms are understood to have the same meaning as commonly used in the art to which they pertain. For the purpose of the present invention, the following terms are defined below.

In the context of the invention, the term "gene expression system" refers to any system, device or means to detect gene expression and includes diagnostic agents, candidate libraries, oligonucleotide sets or probe sets.

The term "monitoring" is used herein to describe the use of gene sets to provide useful information about an individual or an individual's health or disease status. "Monitoring" can include, determination of prognosis, risk-stratification, selection of drug therapy, assessment of ongoing drug therapy, prediction of outcomes, determining response to therapy, diagnosis of a disease or disease complication, following progression of a disease or providing any information relating to a patients health status over time, selecting patients most likely to benefit from experimental therapies with known molecular mechanisms of action, selecting patients most likely to benefit from approved drugs with known molecular mechanisms where that mechanism may be important in a small subset of a disease for which the medication may not have a label, screening a patient population to help decide on a more invasive/expensive test, for example a cascade of tests from a non-invasive blood test to a more invasive option such as biopsy, or testing to assess side effects of drugs used to treat another indication..

The term "diagnostic oligonucleotide set" generally refers to a set of two or more oligonucleotides that, when evaluated for differential expression of their products, collectively yields predictive data. Such predictive data typically relates to diagnosis, prognosis, monitoring of therapeutic outcomes, and the like. In general, the components of a diagnostic oligonucleotide set are distinguished from nucleotide sequences that are evaluated by analysis of the DNA to directly determine the genotype of an individual as it correlates with a specified trait or phenotype, such as a disease, in that it is the pattern of expression of the components of the diagnostic nucleotide set, rather than mutation or polymorphism of the DNA sequence that provides predictive value. It will be understood that a particular component (or member) of a diagnostic nucleotide set can, in some cases, also present one or more mutations, or polymorphisms that are amenable to direct genotyping by any of a variety of well known analysis methods, e.g., Southern blotting, RFLP, AFLP, SSCP, SNP, and the like.

A "disease specific target oligonucleotide sequence" is a gene or other oligonucleotide that encodes a polypeptide, most typically a protein, or a subunit of a multi-subunit protein, that is a therapeutic target for a disease, or group of diseases.

A "candidate library" or a "candidate oligonucleotide library" refers to a collection of oligonucleotide sequences (or gene sequences) that by one or more criteria have an increased probability of being associated with a particular disease or group of diseases. The criteria can be, for

example, a differential expression pattern in a disease state or in activated or resting leukocytes in vitro as reported in the scientific or technical literature, tissue specific expression as reported in a sequence database, differential expression in a tissue or cell type of interest, or the like. Typically, a candidate library has at least 2 members or components; more typically, the library has in excess of about 10, or about 100, or about 1000, or even more, members or components.

The term "disease criterion" is used herein to designate an indicator of a disease, such as a diagnostic factor, a prognostic factor, a factor indicated by a medical or family history, a genetic factor, or a symptom, as well as an overt or confirmed diagnosis of a disease associated with several indicators such as those selected from the above list. A disease criterian includes data describing a patient's health status, including retrospective or prospective health data, e.g. in the form of the patient's medical history, laboratory test results, diagnostic test result, clinical events, medications, lists, response(s) to treatment and risk factors, etc.

The terms "molecular signature" or "expression profile" refers to the collection of expression values for a plurality (e.g., at least 2, but frequently about 10, about 100, about 1000, or more) of members of a candidate library. In many cases, the molecular signature represents the expression pattern for all of the nucleotide sequences in a library or array of candidate or diagnostic nucleotide sequences or genes. Alternatively, the molecular signature represents the expression pattern for one or more subsets of the candidate library. The term "oligonucleotide" refers to two or more nucleotides. Nucleotides may be DNA or RNA, naturally occurring or synthetic.

The term "healthy individual," as used herein, is relative to a specified disease or disease criterion. That is, the individual does not exhibit the specified disease criterion or is not diagnosed with the specified disease. It will be understood, that the individual in question, can, of course, exhibit symptoms, or possess various indicator factors for another disease.

Similarly, an "individual diagnosed with a disease" refers to an individual diagnosed with a specified disease (or disease criterion). Such an individual may, or may not, also exhibit a disease criterion associated with, or be diagnosed with another (related or unrelated) disease.

An "array" is a spatially or logically organized collection, e.g., of oligonucleotide sequences or nucleotide sequence products such as RNA or proteins encoded by an oligonucleotide sequence. In some embodiments, an array includes antibodies or other binding reagents specific for products of a candidate library.

When referring to a pattern of expression, a "qualitative" difference in gene expression refers to a difference that is not assigned a relative value. That is, such a difference is designated by an "all or nothing" valuation. Such an all or nothing variation can be, for example, expression above or below a threshold of detection (an on/off pattern of expression). Alternatively, a qualitative difference can refer to expression of different types of expression products, e.g., different alleles (e.g., a mutant or polymorphic allele), variants (including sequence variants as well as post-translationally modified variants), etc.

In contrast, a "quantitative" difference, when referring to a pattern of gene expression, refers to a difference in expression that can be assigned a value on a graduated scale, (e.g., a 0-5 or 1-10 scale, a + - +++ scale, a grade 1- grade 5 scale, or the like; it will be understood that the numbers

selected for illustration are entirely arbitrary and in no-way are meant to be interpreted to limit the invention).

Gene Expression Systems of the Invention

The invention is directed to a gene expression system having one or more DNA molecules wherein the one or more DNA molecules has a nucleotide sequence which detects expression of a gene corresponding to the oligonucleotides depicted in the Sequence Listing. In one format, the oligonucleotide detects expression of a gene that is differentially expressed in leukocytes. The gene expression system may be a candidate library, a diagnostic agent, a diagnostic oligonucleotide set or a diagnostic probe set. The DNA molecules may be genomic DNA, protein nucleic acid (PNA), cDNA or synthetic oligonucleotides. Following the procedures taught herein, one can identity sequences of interest for analyzing gene expression in leukocytes. Such sequences may be predictive of a disease state.

Diagnostic oligonucleotides of the invention

The invention relates to diagnostic nucleotide set(s) comprising members of the leukocyte candidate library listed in Table 2, Table 8, and in the Sequence Listing, for which a correlation exists between the health status of an individual, the individual's expression of RNA or protein products corresponding to the nucleotide sequence, and the diagnosis and prognosis of transplant rejection. In some instances, only one oligonucleotide is necessary for such detection. Members of a diagnostic oligonucleotide set may be identified by any means capable of detecting expression of RNA or protein products, including but not limited to differential expression screening, PCR, RT-PCR, SAGE analysis, high-throughput sequencing, microarrays, liquid or other arrays, protein-based methods (e.g., western blotting, proteomics, and other methods described herein), and data mining methods, as further described herein.

In one embodiment, a diagnostic oligonucleotide set comprises at least two oligonucleotide sequences listed in Table 2, Table 8, or the Sequence Listing which are differentially expressed in leukocytes in an individual with at least one disease criterion for at least one leukocyte-implicated disease relative to the expression in individual without the at least one disease criterion, wherein expression of the two or more nucleotide sequences is correlated with at least one disease criterion, as described below.

In another embodiment, a diagnostic nucleotide set comprises at least one oligonucleotide having an oligonucleotide sequence listed in Table 2, Table 8, or the Sequence Listing which is differentially expressed, and further wherein the differential expression/correlation has not previously been described. In some embodiments, the diagnostic nucleotide set is immobilized on an array.

In another embodiment, diagnostic nucleotides (or nucleotide sets) are related to the members of the leukocyte candidate library listed in Table 2, Table 8, or in the Sequence Listing, for which a correlation exists between the health status, diagnosis and prognosis of transplant rejection (or disease criterion) of an individual. The diagnostic nucleotides are partially or totally contained in (or derived from) full-length gene sequences (or predicted full-length gene sequences) for the members of the candidate library listed in Table 2, Table 8, and the sequence listing. In some cases, oligonucleotide sequences are designed from EST or Chromosomal sequences from a public database. In these cases

the full-length gene sequences may not be known. Full-length sequences in these cases can be predicted using gene prediction algorithms. Alternatively the full-length can be determined by cloning and sequencing the full-length gene or genes that contain the sequence of interest using standard molecular biology approaches described here. The same is true for olignonucleotides designed from our sequencing of cDNA libraries where the cDNA does not match any sequence in the public databases.

The diagnostic nucleotides may also be derived from other genes that are coexpressed with the correlated sequence or full-length gene. Genes may share expression patterns because they are regulated in the same molecular pathway. Because of the similarity of expression behavior genes are identified as surrogates in that they can substitute for a diagnostic gene in a diagnostic gene set. Example 4 demonstrates the discovery of surrogates from the data and the sequence listing identifies and gives the sequence for surrogates for cardiac diagnostic genes.

As used herein the term "gene cluster" or "cluster" refers to a group of genes related by expression pattern. In other words, a cluster of genes is a group of genes with similar regulation across different conditions, such as graft non-rejection verus graft rejection. The expression profile for each gene in a cluster should be correlated with the expression profile of at least one other gene in that cluster. Correlation may be evaluated using a variety of statistical methods. As used herein the term "surrogate" refers to a gene with an expression profile such that it can substitute for a diagnostic gene in a diagnostic assay. Such genes are often members of the same gene cluster as the diagnostic gene. For each member of a diagnostic gene set, a set of potential surrogates can be identified through identification of genes with similar expression patterns as described below.

Many statistical analyses produce a correlation coefficient to describe the relatedness between two gene expression patterns. Patterns may be considered correlated if the correlation coefficient is greater than or equal to 0.8. In preferred embodiments, the correlation coefficient should be greater than 0.85, 0.9 or 0.95. Other statistical methods produce a measure of mutual information to describe the relatedness between two gene expression patterns. Patterns may be considered correlated if the normalized mutual information value is greater than or equal to 0.7. In preferred embodiments, the normalized mutual information value should be greater than 0.8, 0.9 or 0.95. Patterns may also be considered similar if they cluster closely upon hierarchical clustering of gene expression data (Eisen et al. 1998). Similar patterns may be those genes that are among the 1, 2, 5, 10, 20, 50 or 100 nearest neighbors in a hierarchical clustering or have a similarity score (Eisen et al. 1998) of > 0.5, 0.7, 0.8, 0.9, 0.95 or 0.99. Similar patterns may also be identified as those genes found to be surrogates in a classification tree by CART (Breiman et al. 1994). Often, but not always, members of a gene cluster have similar biological functions in addition to similar gene expression patterns.

Correlated genes, clusters and surrogates are identified for the diagnostic genes of the invention. These surrogates may be used as diagnostic genes in an assay instead of, or in addition to, the diagnostic genes for which they are surrogates.

The invention also provides diagnostic probe sets. It is understood that a probe includes any reagent capable of specifically identifying a nucleotide sequence of the diagnostic nucleotide set, including but not limited to amplified DNA, amplified RNA, cDNA, synthetic oligonucleotide, partial

or full-length nucleic acid sequences. In addition, the probe may identify the protein product of a diagnostic nucleotide sequence, including, for example, antibodies and other affinity reagents.

It is also understood that each probe can correspond to one gene, or multiple probes can correspond to one gene, or both, or one probe can correspond to more than one gene.

Homologs and variants of the disclosed nucleic acid molecules may be used in the present invention. Homologs and variants of these nucleic acid molecules will possess a relatively high degree of sequence identity when aligned using standard methods. The sequences encompassed by the invention have at least 40-50, 50-60, 70-80, 80-85, 85-90, 90-95 or 95-100% sequence identity to the sequences disclosed herein.

It is understood that for expression profiling, variations in the disclosed sequences will still permit detection of gene expression. The degree of sequence identity required to detect gene expression varies depending on the length of the oligomer. For a 60 mer, 6-8 random mutations or 6-8 random deletions in a 60 mer do not affect gene expression detection. Hughes, TR, et al. "Expression profiling using microarrays fabricated by an ink-jet oligonucleotide synthesizer. Nature Biotechnology, 19:343-347(2001). As the length of the DNA sequence is increased, the number of mutations or deletions permitted while still allowing gene expression detection is increased.

As will be appreciated by those skilled in the art, the sequences of the present invention may contain sequencing errors. That is, there may be incorrect nucleotides, frameshifts, unknown nucleotides, or other types of sequencing errors in any of the sequences; however, the correct sequences will fall within the homology and stringency definitions herein.

The minimum length of an oligonucleotide probe necessary for specific hybridization in the human genome can be estimated using two approaches. The first method uses a statistical argument that the probe will be unique in the human genome by chance. Briefly, the number of independent perfect matches (Po) expected for an oligonucleotide of length L in a genome of complexity C can be · calculated from the equation (Laird CD, Chromosoma 32:378 (1971):

$$Po=(1/4)^L * 2C$$

In the case of mammalian genomes, $2C = \sim3.6 \times 10^9$, and an oligonucleotide of 14-15 nucleotides is expected to be represented only once in the genome. However, the distribution of nucleotides in the coding sequence of mammalian genomes is nonrandom (Lathe, R. J. Mol. Biol. 183:1 (1985) and longer oligonucleotides may be preferred in order to in increase the specificity of hybridization. In practical terms, this works out to probes that are 19-40 nucleotides long (Sambrook J et al., infra). The second method for estimating the length of a specific probe is to use a probe long enough to hybridize under the chosen conditions and use a computer to search for that sequence or close matches to the sequence in the human genome and choose a unique match. Probe sequences are chosen based on the desired hybridization properties as described in Chapter 11 of Sambrook et al, infra. The PRIMER3 program is useful for designing these probes (S. Rozen and H. Skaletsky 1996,1997; Primer3 code available at the web site located at genome.wi.mit.edu/genome_software/other/primer3.html). The sequences of these probes are then compared pair wise against a database of the human genome sequences using a program such as BLAST or MEGABLAST (Madden, T.L et al.(1996) Meth. Enzymol. 266:131-141). Since most of the

human genome is now contained in the database, the number of matches will be determined. Probe sequences are chosen that are unique to the desired target sequence.

In some embodiments, a diagnostic probe set is immobilized on an array. The array is optionally comprises one or more of: a chip array, a plate array, a bead array, a pin array, a membrane array, a solid surface array, a liquid array, an oligonucleotide array, a polynucleotide array or a cDNA array, a microtiter plate, a pin array, a bead array, a membrane or a chip.

In some embodiments, the leukocyte-implicated disease is selected from the diseases listed in Table 1. In other embodiments, In some embodiments, the disease is atherosclerosis or cardiac allograft rejection. In other embodiments, the disease is congestive heart failure, angina, and myocardial infarction.

In some embodiments, diagnostic nucleotides of the invention are used as a diagnostic gene set in combination with genes that are know to be associated with a disease state ("known markers"). The use of the diagnostic nucleotides in combination with the known markers can provide information that is not obtainable through the known markers alone. The known markers include those identified by the prior art listing provided.

Hematopoeisis

The present invention is also directed to methods of measurement of the rate of hematopoiesis using the diagnostic oligonucleotides of the invention and measurement of the rates of hematopoesis by any technique as a method for the monitoring and diagnosis of transplant rejection. Precursor and immature cells often have cell specific phenotypic markers. These are genes and/or proteins that expressed in a restricted manner in immature or precursor cells. This expression decreases with maturation. Gene expression markers for immature cells of a variety of lineages are given in Table 10 below by way of example.

Table 10:

Gene	Cell type
CD10	B-lymphoblasts
RAG1	B-lymphoblasts
RAG2	B-lymphoblasts
NF-E2	Platelets/Megakaryocyte/Erythroid
GATA-1	Platelets/Megakaryocyte
GP IIb	Platelets
pf4	Platelets
EPO-R	Erythroblast
Band 4.1	Erythrocyte
ALAS2	Erythroid specific heme biosynthesis
hemoglobin chains	Erythocyte
2,3-BPG mutase	Erythrocyte
CD16b	Neutrophil
LAP	Neutrophil
CD16	NK cells
CD159a	NK cells

By measuring the levels of these and other genes in peripheral blood samples, an assessment of the number and proportion of immature or precursor cells can be made. Of particular use is RNA quantification in erythrocytes and platelets. These cells are anucleated in their mature forms. During

development, platelets pinch off of a megakaryocyte and take a compliment of RNA without a nucleus. This RNA is quickly consumed by the platelet. Erythrocytes start as nucleated cells, but the nucleus extrudes toward the end of the maturation process. These cells have RNA which is rapidly consumed within the first 2 days of the cells 120 day life span.

For these anucleated cell types, gene expression markers must be specific only to the cell line (and not the immature form) to be useful as measures of cellular production rates. Genes specific to the lineage vs. other blood cell types will serve as markers of cellular production rates when measured on the RNA level. This is because RNA is specific to immature forms in these cases. For example, hemoglobin is specific to erythrocytes, but hemoglobin RNA is specific to newly produced erythrocytes. Therefore, if the rate of production of erythrocytes increases, so will the level of a lineage specific RNA (e.g., hemoglobin).

Hematopoietic growth factors and cytokines have incomplete lineage specificity. G-CSF is administered to patient with low granulocyte counts and the effect is a stimulation of all lineages (granulocytes, erythrocytes, platelets, etc...). Hemolytic anemia leads to increased production of multiple cell lineages although the only lineage in increased demand is the erythrocyte. Because of this lack of specificity of hematopoietic responses, erythrocyte and platelet production rates may serve as surrogates of increased production of lymphocyte lineages. Using RBCs and platelets production rates as surrogates for lymphocyte lineages may be useful because of the lack of a nucleus in these cells and the ease of measuring cellular production rates by simply measuring lineage specific RNA levels.

Hematopoieis rates can be measured using gene expression profiling of peripheral blood. RBC and platelet specific genes provide unique opportunity for this because of their lack of a nucleus and kinetics. New cells = new / much more RNA from these cell types in peripheral blood. Immature lymphocytes may be even more specific for immune activation and rejection. Cell specific markers of lymphocyte precursors were identified (aka lymphoblasts) see below. Granulocyte precursors and markers of megakaryocytes or premature forms of any blood cells may be useful in this regard.

Applications for measuring the rate of hematopoiesis

Changes in the rate of hematopoiesis have been correlated to a number of disease states and other pathologies. Examples of such conditions are listed in Table 11. One of skill in the art would be aware of other such conditions. In addition, one aspect of the present invention is the identification of the linkage between changes in the rate of hematopoiesis. The methods of the present invention directed to measuring the rates of hematopoiesis can therefore be applied to the diagnosis and monitoring of a number of disease states and other pathologies. In addition, these methods can be beneficial in determining appropriate therapies for patients.

Table: 11

Disorder / condition	Cell type	Cell production	Therapy
Anemia – Iron Deficiency	Erythrocyte	Decreased	Iron
Anemia – B12, Folate deficiency	Erythrocyte	Decreased	B12, Folate
Anemia – Aplastic	Erythrocyte	Decreased	Epogen, transfusion

Anemia – hemolytic	Erythrocyte	Increased	Immunosuppression, Splenectomy
Anemia – Renal failure	Erythrocyte	Decreased	Erythropoietin
Anemia – Chronic disease	Erythrocyte	Decreased	Treat underlying cause
Polycythemia rubra vera	Erythrocyte	Increased	
Idiophic Thrrombocytopenic purpura	Platelet	Increased	Immunosuppression, Splenectomy
Thrombotic Thrombocytopenic purpura	Platelet	Increased or decreased	Immunosuppression, plasmapheresis
Essential thrombocytosis	Platelet	Increased	
Leukemia	All lineages, variable	Increase, decreased or abnomal	Chemotherapy, BMT
Cytopenias due to immunosupression	All lineages, variable	Decreased	Epo, neupogen
Cytopenias due to Chemotherapy	All lineages, variable	Decreased	Epo, GCSF, GMCSF
GVHD	All lineages, variable	Decreased	Immunosuppression
Myelodysplasia	All lineages, variable	Decreased, increased or abnormal	Chemo?
Allograft rejection	Lymphocytes, All lineages	Increased	Immunosuppression
Autoimmune diseases (many)	Lymphocytes, All lineages	Increased	Immunosuppression

The methods of the present invention are also useful for monitoring treatment regimens of diseases or other pathologies which are correlated with changes in the rate of hematopoiesis. Furthermore, the methods may be used to monitor treatment with agents that affect the rate of hematopoiesis. One of skill in the art is aware of many such agents. The following agents are examples of such.

Erythropoietin is a growth factor that is used to treat a variety of anemias that are due to decreased red cell production. Monitoring of red cell production by gene expression or other means may improve dosing and provide a means for earlier assessment of response to therapy for this expensive drug.

Neupogen (G-CSF) is used for the treatment of low neutrophil counts (neutropenia) usually related to immunosuppression or chemotherapy. Monitoring neutrophil production by gene expression testing or another means may improve dosing, patient selection, and shorten duration of therapy.

Prednisone / Immunosuppression – One of most common side effects of immunosuppression is suppression of hematopoiesis. This may occur in any cell lineage. Gene expression monitoring or other measures of hematopoietic rates could be used to monitor regularly for cytopenias in a particular cell line and the information could be used to modify dosing, modify therapy or add a specific hematologic growth factor. Following cell counts themselves is less sensitive and results in the need for prolonged trials of therapies at a given dose before efficacy and toxicity can be assessed.

Monitoring of chemotherapeutic agents –Most chemotherapy agents suppress the bone marrow for some or all lineages. Gene expression testing or other means of assessing hematopoietic rates could be used to monitor regularly for cytopenias in a particular cell line and use information to modify dosing, modify therapy or add a specific hematologic growth factor.

General Molecular Biology References

In the context of the invention, nucleic acids and/or proteins are manipulated according to well known molecular biology techniques. Detailed protocols for numerous such procedures are described in, e.g., in Ausubel et al. Current Protocols in Molecular Biology (supplemented through 2000) John Wiley & Sons, New York ("Ausubel"); Sambrook et al. Molecular Cloning - A Laboratory Manual (2nd Ed.), Vol. 1-3, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989 ("Sambrook"), and Berger and Kimmel Guide to Molecular Cloning Techniques, Methods in Enzymology volume 152 Academic Press, Inc., San Diego, CA ("Berger").

In addition to the above references, protocols for in vitro amplification techniques, such as the polymerase chain reaction (PCR), the ligase chain reaction (LCR), Q-replicase amplification, and other RNA polymerase mediated techniques (e.g., NASBA), useful e.g., for amplifying cDNA probes of the invention, are found in Mullis et al. (1987) U.S. Patent No. 4,683,202; PCR Protocols A Guide to Methods and Applications (Innis et al. eds) Academic Press Inc. San Diego, CA (1990) ("Innis"); Arnheim and Levinson (1990) C&EN 36; The Journal Of NIH Research (1991) 3:81; Kwoh et al. (1989) Proc Natl Acad Sci USA 86, 1173; Guatelli et al. (1990) Proc Natl Acad Sci USA 87:1874; Lomell et al. (1989) J Clin Chem 35:1826; Landegren et al. (1988) Science 241:1077; Van Brunt (1990) Biotechnology 8:291; Wu and Wallace (1989) Gene 4: 560; Barringer et al. (1990) Gene 89:117, and Sooknanan and Malek (1995) Biotechnology 13:563. Additional methods, useful for cloning nucleic acids in the context of the present invention, include Wallace et al. U.S. Pat. No. 5,426,039. Improved methods of amplifying large nucleic acids by PCR are summarized in Cheng et al. (1994) Nature 369:684 and the references therein.

Certain polynucleotides of the invention, e.g., oligonucleotides can be synthesized utilizing various solid-phase strategies involving mononucleotide- and/or trinucleotide-based phosphoramidite coupling chemistry. For example, nucleic acid sequences can be synthesized by the sequential addition of activated monomers and/or trimers to an elongating polynucleotide chain. See e.g., Caruthers, M.H. et al. (1992) Meth Enzymol 211:3.

In lieu of synthesizing the desired sequences, essentially any nucleic acid can be custom ordered from any of a variety of commercial sources, such as The Midland Certified Reagent Company, The Great American Gene Company ExpressGen, Inc., Operon Technologies, Inc. and many others.

Similarly, commercial sources for nucleic acid and protein microarrays are available, and include, e.g., Agilent Technologies, Palo Alto, CA Affymetrix, Santa Clara,CA ; and others.

One area of relevance to the present invention is hybridization of oligonucleotides. Those of skill in the art differentiate hybridization conditions based upon the stringency of hybridization. For example, highly stringent conditions could include hybridization to filter-bound DNA in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65° C, and washing in 0.1XSSC/0.1%

SDS at 68° C. (Ausubel F. M. et al., eds., 1989, Current Protocols in Molecular Biology, Vol. I, Green Publishing Associates, Inc., and John Wiley & sons, Inc., New York, at p. 2.10.3). Moderate stringency conditions could include, e.g., washing in 0.2XSSC/0.1% SDS at 42°C. (Ausubel et al., 1989, supra).

The invention also includes nucleic acid molecules, preferably DNA molecules, that hybridize to, and are therefore the complements of, the DNA sequences of the present invention. Such hybridization conditions may be highly stringent or less highly stringent, as described above. In instances wherein the nucleic acid molecules are deoxyoligonucleotides ("oligos"), highly stringent conditions may refer, e.g., to washing in 6xSSC/0.05% sodium pyrophosphate at 37°C. (for 14-base oligos), 48°C. (for 17-base oligos), 55°C. (for 20-base oligos), and 60°C. (for 23-base oligos). These nucleic acid molecules may act as target nucleotide sequence antisense molecules, useful, for example, in target nucleotide sequence regulation and/or as antisense primers in amplification reactions of target nucleotide sequence nucleic acid sequences. Further, such sequences may be used as part of ribozyme and/or triple helix sequences, also useful for target nucleotide sequence regulation. Still further, such molecules may be used as components of diagnostic methods whereby the presence of a disease-causing allele, may be detected.

Identification of diagnostic nucleotide sets

<u>Candidate library</u>

Libraries of candidates that are differentially expressed in leukocytes are substrates for the identification and evaluation of diagnostic oligonucleotide sets and disease specific target nucleotide sequences.

The term leukocyte is used generically to refer to any nucleated blood cell that is not a nucleated erythrocyte. More specifically, leukocytes can be subdivided into two broad classes. The first class includes granulocytes, including, most prevalently, neutrophils, as well as eosinophils and basophils at low frequency. The second class, the non-granular or mononuclear leukocytes, includes monocytes and lymphocytes (e.g., T cells and B cells). There is an extensive literature in the art implicating leukocytes, e.g., neutrophils, monocytes and lymphocytes in a wide variety of disease processes, including inflammatory and rheumatic diseases, neurodegenerative diseases (such as Alzheimer's dementia), cardiovascular disease, endocrine diseases, transplant rejection, malignancy and infectious diseases, and other diseases listed in Table 1. Mononuclear cells are involved in the chronic immune response, while granulocytes, which make up approximately 60% of the leukocytes, have a non-specific and stereotyped response to acute inflammatory stimuli and often have a life span of only 24 hours.

In addition to their widespread involvement and/or implication in numerous disease related processes, leukocytes are particularly attractive substrates for clinical and experimental evaluation for a variety of reasons. Most importantly, they are readily accessible at low cost from essentially every potential subject. Collection is minimally invasive and associated with little pain, disability or recovery time. Collection can be performed by minimally trained personnel (e.g., phlebotomists, medical technicians, etc.) in a variety of clinical and non-clinical settings without significant

technological expenditure. Additionally, leukocytes are renewable, and thus available at multiple time points for a single subject.

Assembly of an initial candidate library

The initial candidate library was assembled from a combination of "mining" publication and sequence databases and construction of a differential expression library. Candidate oligonucleotide sequences in the library may be represented by a full-length or partial nucleic acid sequence, deoxyribonucleic acid (DNA) sequence, cDNA sequence, RNA sequence, synthetic oligonucleotides, etc. The nucleic acid sequence can be at least 19 nucleotides in length, at least 25 nucleotides, at least 40 nucleotides, at least 100 nucleotides, or larger. Alternatively, the protein product of a candidate nucleotide sequence may be represented in a candidate library using standard methods, as further described below. In selecting and validatating diagnostic oligonucleotides, an initial library of 8,031 candidate oligonucleotide sequences using nucleic acid sequences of 50 nucleotides in length was constructed as described below.

Candidate nucleotide library of the invention

We identified members of an initial candidate nucleotide library that are differentially expressed in activated leukocytes and resting leukocytes. From that initial candidate nucleotide library, a pool of candidates was selected as listed in Table 2, Table 8, and the seuqnce listing. Accordingly, the invention provides the candidate leukocyte nucleotide library comprising the nucleotide sequences listed in Table 2, Table 8, and in the sequence listing. In another embodiment, the invention provides an candidate library comprising at least one nucleotide sequence listed in Tables 2 and 8 and the sequence listing. In another embodiment, the invention provides an candidate library comprising at least two nucleotide sequences listed in Tables 2 and 8 and the sequence listing. In another embodiment, the at least two nucleotide sequence are at least 19 nucleotides in length, at least 35 nucleotides, at least 40 nucleotides or at least 100 nucleotides. In some embodiments, the nucleotide sequences comprises deoxyribonucleic acid (DNA) sequence, ribonucleic acid (RNA) sequence, synthetic oligonucleotide sequence, or genomic DNA sequence. It is understood that the nucleotide sequences may each correspond to one gene, or that several nucleotide sequences may correspond to one gene, or both.

The invention also provides probes to the candidate nucleotide library. In one embodiment of the invention, the probes comprise at least two nucleotide sequences listed in Table 2, Table 8, or the sequence listing which are differentially expressed in leukocytes in an individual with a least one disease criterion for at least one leukocyte-related disease and in leukocytes in an individual without the at least one disease criterion, wherein expression of the two or more nucleotide sequences is correlated with at least one disease criterion. It is understood that a probe may detect either the RNA expression or protein product expression of the candidate nucleotide library. Alternatively, or in addition, a probe can detect a genotype associated with a candidate nucleotide sequence, as further described below. In another embodiment, the probes for the candidaten ucleotide library are immobilized on an array.

The candidate nucleotide library of the invention is useful in identifying diagnostic nucleotide sets of the invention and is itself a diagnostic nucleotide set of the invention, as described below. The candidate nucleotide sequences may be further characterized, and may be identified as a disease target

nucleotide sequence and/or a novel nucleotide sequence, as described below. The candidate nucleotide sequences may also be suitable for use as imaging reagents, as described below.

Detection of non-leukocyte expressed genes

When measuring gene expression levels in a blood sample, RNAs may be measured that are not derived from leukocytes. Examples are viral genes, free RNAs that have been released from damaged non-leukocyte cell types or RNA from circulating non-leukocyte cell types. For example, in the process of acute allograft rejection, tissue damage may result in release of allograft cells or RNAs derived from allograft cells into the circulation. In the case of cardiac allografts, such transcripts may be specific to muscle (myoglobin) or to cardiac muscle (Troponin I, Toponin T, CK-MB). Presence of cardiac specific mRNAs in peripheral blood may indicate ongoing or recent cardiac cellular damage (resulting from acute rejection). Therefore, such genes may be excellent diagnostic markers for allograft rejection.

Generation of Expression Patterns

RNA, DNA or protein sample procurement

Following identification or assembly of a library of differentially expressed candidate nucleotide sequences, leukocyte expression profiles corresponding to multiple members of the candidate library are obtained. Leukocyte samples from one or more subjects are obtained by standard methods. Most typically, these methods involve trans-cutaneous venous sampling of peripheral blood. While sampling of circulating leukocytes from whole blood from the peripheral vasculature is generally the simplest, least invasive, and lowest cost alternative, it will be appreciated that numerous alternative sampling procedures exist, and are favorably employed in some circumstances. No pertinent distinction exists, in fact, between leukocytes sampled from the peripheral vasculature, and those obtained, e.g., from a central line, from a central artery, or indeed from a cardiac catheter, or during a surgical procedure which accesses the central vasculature. In addition, other body fluids and tissues that are, at least in part, composed of leukocytes are also desirable leukocyte samples. For example, fluid samples obtained from the lung during bronchoscopy may be rich in leukocytes, and amenable to expression profiling in the context of the invention, e.g., for the diagnosis, prognosis, or monitoring of lung transplant rejection, inflammatory lung diseases or infectious lung disease. Fluid samples from other tissues, e.g., obtained by endoscopy of the colon, sinuses, esophagus, stomach, small bowel, pancreatic duct, biliary tree, bladder, ureter, vagina, cervix or uterus, etc., are also suitable. Samples may also be obtained other sources containing leukocytes, e.g., from urine, bile, cerebrospinal fluid, feces, gastric or intestinal secretions, semen, or solid organ or joint biopsies.

Most frequently, mixed populations of leukocytes, such as are found in whole blood are utilized in the methods of the present invention. A crude separation, e.g., of mixed leukocytes from red blood cells, and/or concentration, e.g., over a sucrose, percoll or ficoll gradient, or by other methods known in the art, can be employed to facilitate the recovery of RNA or protein expression products at sufficient concentrations, and to reduce non-specific background. In some instances, it can be desirable to purify sub-populations of leukocytes, and methods for doing so, such as density or affinity gradients, flow cytometry, fluorescence Activated Cell Sorting (FACS), immuno-magnetic separation, "panning," and the like, are described in the available literature and below.

<u>Obtaining DNA, RNA and protein samples for expression profiling</u>

Expression patterns can be evaluated at the level of DNA, or RNA or protein products. For example, a variety of techniques are available for the isolation of RNA from whole blood. Any technique that allows isolation of mRNA from cells (in the presence or absence of rRNA and tRNA) can be utilized. In brief, one method that allows reliable isolation of total RNA suitable for subsequent gene expression analysis, is described as follows. Peripheral blood (either venous or arterial) is drawn from a subject, into one or more sterile, endotoxin free, tubes containing an anticoagulant (e.g., EDTA, citrate, heparin, etc.). Typically, the sample is divided into at least two portions. One portion, e.g., of 5-8 ml of whole blood is frozen and stored for future analysis, e.g., of DNA or protein. A second portion, e.g., of approximately 8 ml whole blood is processed for isolation of total RNA by any of a variety of techniques as described in, e.g, Sambook, Ausubel, below, as well as U.S. Patent Numbers: 5,728,822 and 4,843,155.

Typically, a subject sample of mononuclear leukocytes obtained from about 8 ml of whole blood, a quantity readily available from an adult human subject under most circumstances, yields 5-20 µg of total RNA. This amount is ample, e.g., for labeling and hybridization to at least two probe arrays. Labeled probes for analysis of expression patterns of nucleotides of the candidate libraries are prepared from the subject's sample of RNA using standard methods. In many cases, cDNA is synthesized from total RNA using a polyT primer and labeled, e.g., radioactive or fluorescent, nucleotides. The resulting labeled cDNA is then hybridized to probes corresponding to members of the candidate nucleotide library, and expression data is obtained for each nucleotide sequence in the library. RNA isolated from subject samples (e.g., peripheral blood leukocytes, or leukocytes obtained from other biological fluids and samples) is next used for analysis of expression patterns of nucleotides of the candidate libraries.

In some cases, however, the amount of RNA that is extracted from the leukocyte sample is limiting, and amplification of the RNA is desirable. Amplification may be accomplished by increasing the efficiency of probe labeling, or by amplifying the RNA sample prior to labeling. It is appreciated that care must be taken to select an amplification procedure that does not introduce any bias (with respect to gene expression levels) during the amplification process.

Several methods are available that increase the signal from limiting amounts of RNA, e.g. use of the Clontech (Glass Fluorescent Labeling Kit) or Stratagene (Fairplay Microarray Labeling Kit), or the Micromax kit (New England Nuclear, Inc.). Alternatively, cDNA is synthesized from RNA using a T7- polyT primer, in the absence of label, and DNA dendrimers from Genisphere (3DNA Submicro) are hybridized to the poly T sequence on the primer, or to a different "capture sequence" which is complementary to a fluorescently labeled sequence. Each 3DNA molecule has 250 fluorescent molecules and therefore can strongly label each cDNA.

Alternatively, the RNA sample is amplified prior to labeling. For example, linear amplification may be performed, as described in U.S. Patent No. 6,132,997. A T7-polyT primer is used to generate the cDNA copy of the RNA. A second DNA strand is then made to complete the substrate for amplification. The T7 promoter incorporated into the primer is used by a T7 polymerase to produce numerous antisense copies of the original RNA. Fluorescent dye labeled nucleotides are

directly incorporated into the RNA. Alternatively, amino allyl labeled nucleotides are incorporated into the RNA, and then fluorescent dyes are chemically coupled to the amino allyl groups, as described in Hughes. Other exemplary methods for amplification are described below.

It is appreciated that the RNA isolated must contain RNA derived from leukocytes, but may also contain RNA from other cell types to a variable degree. Additionally, the isolated RNA may come from subsets of leukocytes, e.g. monocytes and/or T-lymphocytes, as described above. Such consideration of cell type used for the derivation of RNA depend on the method of expression profiling used. Subsets of leukocytes can be obtained by fluorescence activated cell sorting (FACS), microfluidics cell seperation systems or a variety of other methods. Cell sorting may be necessary for the discovery of diagnostic gene sets, for the implementation of gene sets as products or both. Cell sorting can be achieved with a variety of technologies (See Galbraith et al. 1999, Cantor et al. 1975, see also the technology of Guava Technologies, Hayward, CA).

DNA samples may be obtained for analysis of the presence of DNA mutations, single nucleotide polymorphisms (SNPs), or other polymorphisms. DNA is isolated using standard techniques, e.g. *Maniatus, supra.*

Expression of products of candidate nucleotides may also be assessed using proteomics. Protein(s) are detected in samples of patient serum or from leukocyte cellular protein. Serum is prepared by centrifugation of whole blood, using standard methods. Proteins present in the serum may have been produced from any of a variety of leukocytes and non-leukocyte cells, and include secreted proteins from leukocytes. Alternatively, leukocytes or a desired sub-population of leukocytes are prepared as described above. Cellular protein is prepared from leukocyte samples using methods well known in the art, e.g., Trizol (Invitrogen Life Technologies, cat # 15596108; Chomczynski, P. and Sacchi, N. (1987) Anal. Biochem. 162, 156; Simms, D., Cizdziel, P.E., and Chomczynski, P. (1993) Focus® 15, 99; Chomczynski, P., Bowers-Finn, R., and Sabatini, L. (1987) J. of NIH Res. 6, 83; Chomczynski, P. (1993) Bio/Techniques 15, 532; Bracete, A.M., Fox, D.K., and Simms, D. (1998) Focus 20, 82; Sewall, A. and McRae, S. (1998) Focus 20, 36; Anal Biochem 1984 Apr;138(1):141-3, A method for the quantitative recovery of protein in dilute solution in the presence of detergents and lipids; Wessel D, Flugge UI. (1984) Anal Biochem. 1984 Apr;138(1):141-143.

The assay itself may be a cell sorting assay in which cells are sorted and/or counted based on cell surface expression of a protein marker. (See Cantor et al. 1975, Galbraith et al. 1999)

Obtaining expression patterns

Expression patterns, or profiles, of a plurality of nucleotides corresponding to members of the candidate library are then evaluated in one or more samples of leukocytes. Typically, the leukocytes are derived from patient peripheral blood samples, although, as indicated above, many other sample sources are also suitable. These expression patterns constitute a set of relative or absolute expression values for a some number of RNAs or protein products corresponding to the plurality of nucleotide sequences evaluated, which is referred to herein as the subject's "expression profile" for those nucleotide sequences. While expression patterns for as few as one independent member of the candidate library can be obtained, it is generally preferable to obtain expression patterns corresponding to a larger number of nucleotide sequences, e.g., about 2, about 5, about 10, about 20, about 50, about

100, about 200, about 500, or about 1000, or more. The expression pattern for each differentially expressed component member of the library provides a finite specificity and sensitivity with respect to predictive value, e.g., for diagnosis, prognosis, monitoring, and the like.

Clinical Studies, Data and Patient Groups

For the purpose of discussion, the term subject, or subject sample of leukocytes, refers to an individual regardless of health and/or disease status. A subject can be a patient, a study participant, a control subject, a screening subject, or any other class of individual from whom a leukocyte sample is obtained and assessed in the context of the invention. Accordingly, a subject can be diagnosed with a disease, can present with one or more symptom of a disease, or a predisposing factor, such as a family (genetic) or medical history (medical) factor, for a disease, or the like. Alternatively, a subject can be healthy with respect to any of the aforementioned factors or criteria. It will be appreciated that the term "healthy" as used herein, is relative to a specified disease, or disease factor, or disease criterion, as the term "healthy" cannot be defined to correspond to any absolute evaluation or status. Thus, an individual defined as healthy with reference to any specified disease or disease criterion, can in fact be diagnosed with any other one or more disease, or exhibit any other one or more disease criterion.

Furthermore, while the discussion of the invention focuses, and is exemplified using human sequences and samples, the invention is equally applicable, through construction or selection of appropriate candidate libraries, to non-human animals, such as laboratory animals, e.g., mice, rats, guinea pigs, rabbits; domesticated livestock, e.g., cows, horses, goats, sheep, chicken, etc.; and companion animals, e.g., dogs, cats, etc.

Methods for obtaining expression data

Numerous methods for obtaining expression data are known, and any one or more of these techniques, singly or in combination, are suitable for determining expression profiles in the context of the present invention. For example, expression patterns can be evaluated by northern analysis, PCR, RT-PCR, Taq Man analysis, FRET detection, monitoring one or more molecular beacon, hybridization to an oligonucleotide array, hybridization to a cDNA array, hybridization to a polynucleotide array, hybridization to a liquid microarray, hybridization to a microelectric array, molecular beacons, cDNA sequencing, clone hybridization, cDNA fragment fingerprinting, serial analysis of gene expression (SAGE), subtractive hybridization, differential display and/or differential screening (see, e.g., Lockhart and Winzeler (2000) Nature 405:827-836, and references cited therein).

For example, specific PCR primers are designed to a member(s) of an candidate nucleotide library. cDNA is prepared from subject sample RNA by reverse transcription from a poly-dT oligonucleotide primer, and subjected to PCR. Double stranded cDNA may be prepared using primers suitable for reverse transcription of the PCR product, followed by amplification of the cDNA using in vitro transcription. The product of in vitro transcription is a sense-RNA corresponding to the original member(s) of the candidate library. PCR product may be also be evaluated in a number of ways known in the art, including real-time assessment using detection of labeled primers, e.g. TaqMan or molecular beacon probes. Technology platforms suitable for analysis of PCR products include the ABI 7700, 5700, or 7000 Sequence Detection Systems (Applied Biosystems, Foster City, CA), the MJ Research Opticon (MJ Research, Waltham, MA), the Roche Light Cycler (Roche Diagnositics, Indianapolis, IN),

the Stratagene MX4000 (Stratagene, La Jolla, CA), and the Bio-Rad iCycler (Bio-Rad Laboratories, Hercules, CA). Alternatively, molecular beacons are used to detect presence of a nucleic acid sequence in an unamplified RNA or cDNA sample, or following amplification of the sequence using any method, e.g. IVT (In Vitro transcription) or NASBA (nucleic acid sequence based amplification). Molecular beacons are designed with sequences complementary to member(s) of an candidate nucleotide library, and are linked to fluorescent labels. Each probe has a different fluorescent label with non-overlapping emission wavelengths. For example, expression of ten genes may be assessed using ten different sequence-specific molecular beacons.

Alternatively, or in addition, molecular beacons are used to assess expression of multiple nucleotide sequences at once. Molecular beacons with sequence complimentary to the members of a diagnostic nucleotide set are designed and linked to fluorescent labels. Each fluorescent label used must have a non-overlapping emission wavelength. For example, 10 nucleotide sequences can be assessed by hybridizing 10 sequence specific molecular beacons (each labeled with a different fluorescent molecule) to an amplified or un-amplified RNA or cDNA sample. Such an assay bypasses the need for sample labeling procedures.

Alternatively, or in addition bead arrays can be used to assess expression of multiple sequences at once. See, e.g, LabMAP 100, Luminex Corp, Austin, Texas). Alternatively, or in addition electric arrays are used to assess expression of multiple sequences, as exemplified by the e-Sensor technology of Motorola (Chicago, Ill.) or Nanochip technology of Nanogen (San Diego, CA.)

Of course, the particular method elected will be dependent on such factors as quantity of RNA recovered, practitioner preference, available reagents and equipment, detectors, and the like. Typically, however, the elected method(s) will be appropriate for processing the number of samples and probes of interest. Methods for high-throughput expression analysis are discussed below.

Alternatively, expression at the level of protein products of gene expression is performed. For example, protein expression, in a sample of leukocytes, can be evaluated by one or more method selected from among: western analysis, two-dimensional gel analysis, chromatographic separation, mass spectrometric detection, protein-fusion reporter constructs, colorimetric assays, binding to a protein array and characterization of polysomal mRNA. One particularly favorable approach involves binding of labeled protein expression products to an array of antibodies specific for members of the candidate library. Methods for producing and evaluating antibodies are widespread in the art, see, e.g., Coligan, supra; and Harlow and Lane (1989) Antibodies: A Laboratory Manual, Cold Spring Harbor Press, NY ("Harlow and Lane"). Additional details regarding a variety of immunological and immunoassay procedures adaptable to the present invention by selection of antibody reagents specific for the products of candidate nucleotide sequences can be found in, e.g., Stites and Terr (eds.)(1991) Basic and Clinical Immunology, 7th ed., and Paul, supra. Another approach uses systems for performing desorption spectrometry. Commercially available systems, e.g., from Ciphergen Biosystems, Inc. (Fremont, CA) are particularly well suited to quantitative analysis of protein expression. Indeed, Protein Chip® arrays (see, e.g., the web site ciphergen.com) used in desorption spectrometry approaches provide arrays for detection of protein expression. Alternatively, affinity reagents, e.g., antibodies, small molecules, etc.) are developed that recognize epitopes of the protein

product. Affinity assays are used in protein array assays, e.g. to detect the presence or absence of particular proteins. Alternatively, affinity reagents are used to detect expression using the methods described above. In the case of a protein that is expressed on the cell surface of leukocytes, labeled affinity reagents are bound to populations of leukocytes, and leukocytes expressing the protein are identified and counted using fluorescent activated cell sorting (FACS).

It is appreciated that the methods of expression evaluation discussed herein, although discussed in the context of discovery of diagnostic nucleotide sets, are equally applicable for expression evaluation when using diagnostic nucleotide sets for, e.g. diagnosis of diseases, as further discussed below.

High Throughput Expression Assays

A number of suitable high throughput formats exist for evaluating gene expression. Typically, the term high throughput refers to a format that performs at least about 100 assays, or at least about 500 assays, or at least about 1000 assays, or at least about 5000 assays, or at least about 10,000 assays, or more per day. When enumerating assays, either the number of samples or the number of candidate nucleotide sequences evaluated can be considered. For example, a northern analysis of, e.g., about 100 samples performed in a gridded array, e.g., a dot blot, using a single probe corresponding to an candidate nucleotide sequence can be considered a high throughput assay. More typically, however, such an assay is performed as a series of duplicate blots, each evaluated with a distinct probe corresponding to a different member of the candidate library. Alternatively, methods that simultaneously evaluate expression of about 100 or more candidate nucleotide sequences in one or more samples, or in multiple samples, are considered high throughput.

Numerous technological platforms for performing high throughput expression analysis are known. Generally, such methods involve a logical or physical array of either the subject samples, or the candidate library, or both. Common array formats include both liquid and solid phase arrays. For example, assays employing liquid phase arrays, e.g., for hybridization of nucleic acids, binding of antibodies or other receptors to ligand, etc., can be performed in multiwell, or microtiter, plates. Microtiter plates with 96, 384 or 1536 wells are widely available, and even higher numbers of wells, e.g, 3456 and 9600 can be used. In general, the choice of microtiter plates is determined by the methods and equipment, e.g., robotic handling and loading systems, used for sample preparation and analysis. Exemplary systems include, e.g., the ORCA™ system from Beckman-Coulter, Inc. (Fullerton, CA) and the Zymate systems from Zymark Corporation (Hopkinton, MA).

Alternatively, a variety of solid phase arrays can favorably be employed in to determine expression patterns in the context of the invention. Exemplary formats include membrane or filter arrays (e.g, nitrocellulose, nylon), pin arrays, and bead arrays (e.g., in a liquid "slurry"). Typically, probes corresponding to nucleic acid or protein reagents that specifically interact with (e.g., hybridize to or bind to) an expression product corresponding to a member of the candidate library are immobilized, for example by direct or indirect cross-linking, to the solid support. Essentially any solid support capable of withstanding the reagents and conditions necessary for performing the particular expression assay can be utilized. For example, functionalized glass, silicon, silicon dioxide, modified silicon, any of a variety of polymers, such as (poly)tetrafluoroethylene, (poly)vinylidenedifluoride,

polystyrene, polycarbonate, or combinations thereof can all serve as the substrate for a solid phase
array.

In a preferred embodiment, the array is a "chip" composed, e.g., of one of the above specified
materials. Polynucleotide probes, e.g., RNA or DNA, such as cDNA, synthetic oligonucleotides, and
the like, or binding proteins such as antibodies, that specifically interact with expression products of
individual components of the candidate library are affixed to the chip in a logically ordered manner,
i.e., in an array. In addition, any molecule with a specific affinity for either the sense or anti-sense
sequence of the marker nucleotide sequence (depending on the design of the sample labeling), can be
fixed to the array surface without loss of specific affinity for the marker and can be obtained and
produced for array production, for example, proteins that specifically recognize the specific nucleic
acid sequence of the marker, ribozymes, peptide nucleic acids (PNA), or other chemicals or molecules
with specific affinity.

Detailed discussion of methods for linking nucleic acids and proteins to a chip substrate, are
found in, e.g., US Patent No. 5,143,854 "LARGE SCALE PHOTOLITHOGRAPHIC SOLID PHASE
SYNTHESIS OF POLYPEPTIDES AND RECEPTOR BINDING SCREENING THEREOF" to
Pirrung et al., issued, September 1, 1992; US Patent No. 5,837,832 "ARRAYS OF NUCLEIC ACID
PROBES ON BIOLOGICAL CHIPS" to Chee et al., issued November 17, 1998; US Patent No.
6,087,112 "ARRAYS WITH MODIFIED OLIGONUCLEOTIDE AND POLYNUCLEOTIDE
COMPOSITIONS" to Dale, issued July 11, 2000; US Patent No. 5,215,882 "METHOD OF
IMMOBILIZING NUCLEIC ACID ON A SOLID SUBSTRATE FOR USE IN NUCLEIC ACID
HYBRIDIZATION ASSAYS" to Bahl et al., issued June 1, 1993; US Patent No. 5,707,807
"MOLECULAR INDEXING FOR EXPRESSED GENE ANALYSIS" to Kato, issued January 13,
1998; US Patent No. 5,807,522 "METHODS FOR FABRICATING MICROARRAYS OF
BIOLOGICAL SAMPLES" to Brown et al., issued September 15, 1998; US Patent No. 5,958,342
"JET DROPLET DEVICE" to Gamble et al., issued Sept. 28, 1999; US Patent 5,994,076 "METHODS
OF ASSAYING DIFFERENTIAL EXPRESSION" to Chenchik et al., issued Nov. 30, 1999; US Patent
No. 6,004,755 "QUANTITATIVE MICROARRAY HYBRIDIZATION ASSAYS" to Wang, issued
Dec. 21, 1999; US Patent No. 6,048,695 "CHEMICALLY MODIFIED NUCLEIC ACIDS AND
METHOD FOR COUPLING NUCLEIC ACIDS TO SOLID SUPPORT" to Bradley et al., issued April
11, 2000; US Patent No. 6,060,240 "METHODS FOR MEASURING RELATIVE AMOUNTS OF
NUCLEIC ACIDS IN A COMPLEX MIXTURE AND RETRIEVAL OF SPECIFIC SEQUENCES
THEREFROM" to Kamb et al., issued May 9, 2000; US Patent No. 6,090,556 "METHOD FOR
QUANTITATIVELY DETERMINING THE EXPRESSION OF A GENE" to Kato, issued July 18,
2000; and US Patent 6,040,138 "EXPRESSION MONITORING BY HYBRIDIZATION TO HIGH
DENSITY OLIGONUCLEOTIDE ARRAYS" to Lockhart et al., issued March 21, 2000 each of which
are hereby incorporated by reference in their entirety.

For example, cDNA inserts corresponding to candidate nucleotide sequences, in a standard
TA cloning vector are amplified by a polymerase chain reaction for approximately 30-40 cycles. The
amplified PCR products are then arrayed onto a glass support by any of a variety of well known
techniques, e.g., the VSLIPS™ technology described in US Patent No. 5,143,854. RNA, or cDNA

corresponding to RNA, isolated from a subject sample of leukocytes is labeled, e.g., with a fluorescent tag, and a solution containing the RNA (or cDNA) is incubated under conditions favorable for hybridization, with the "probe" chip. Following incubation, and washing to eliminate non-specific hybridization, the labeled nucleic acid bound to the chip is detected qualitatively or quantitatively, and the resulting expression profile for the corresponding candidate nucleotide sequences is recorded. It is appreciated that the probe used for diagnostic purposes may be identical to the probe used during diagnostic nucleotide sequence discovery and validation. Alternatively, the probe sequence may be different than the sequence used in diagnostic nucleotide sequence discovery and validation. Multiple cDNAs from a nucleotide sequence that are non-overlapping or partially overlapping may also be used.

In another approach, oligonucleotides corresponding to members of an candidate nucleotide library are synthesized and spotted onto an array. Alternatively, oligonucleotides are synthesized onto the array using methods known in the art, e.g. Hughes, et al. *supra*. The oligonucleotide is designed to be complementary to any portion of the candidate nucleotide sequence. In addition, in the context of expression analysis for, e.g. diagnostic use of diagnostic nucleotide sets, an oligonucleotide can be designed to exhibit particular hybridization characteristics, or to exhibit a particular specificity and/or sensitivity, as further described below.

Hybridization signal may be amplified using methods known in the art, and as described herein, for example use of the Clontech kit (Glass Fluorescent Labeling Kit), Stratagene kit (Fairplay Microarray Labeling Kit), the Micromax kit (New England Nuclear, Inc.), the Genisphere kit (3DNA Submicro), linear amplification, e.g. as described in U.S. Patent No. 6,132,997 or described in Hughes, TR, et al., Nature Biotechnology, 19:343-347 (2001) and/or Westin et al. Nat Biotech. 18:199-204.

Alternatively, fluorescently labeled cDNA are hybridized directly to the microarray using methods known in the art. For example, labeled cDNA are generated by reverse transcription using Cy3- and Cy5-conjugated deoxynucleotides, and the reaction products purified using standard methods. It is appreciated that the methods for signal amplification of expression data useful for identifying diagnostic nucleotide sets are also useful for amplification of expression data for diagnostic purposes.

Microarray expression may be detected by scanning the microarray with a variety of laser or CCD-based scanners, and extracting features with numerous software packages, for example, Imagene (Biodiscovery), Feature Extraction (Agilent), Scanalyze (Eisen, M. 1999. SCANALYZE User Manual; Stanford Univ., Stanford, CA. Ver 2.32.), GenePix (Axon Instruments).

In another approach, hybridization to microelectric arrays is performed, e.g. as described in Umek et al (2001) J Mol Diagn. 3:74-84. An affinity probe, e.g. DNA, is deposited on a metal surface. The metal surface underlying each probe is connected to a metal wire and electrical signal detection system. Unlabelled RNA or cDNA is hybridized to the array, or alternatively, RNA or cDNA sample is amplified before hybridization, e.g. by PCR. Specific hybridization of sample RNA or cDNA results in generation of an electrical signal, which is transmitted to a detector. See Westin (2000) Nat Biotech. 18:199-204 (describing anchored multiplex amplification of a microelectronic chip array); Edman (1997) NAR 25:4907-14; Vignali (2000) J Immunol Methods 243:243-55.

In another approach, a microfluidics chip is used for RNA sample preparation and analysis. This approach increases efficiency because sample preparation and analysis are streamlined. Briefly,

microfluidics may be used to sort specific leukocyte sub-populations prior to RNA preparation and analysis. Microfluidics chips are also useful for, e.g., RNA preparation, and reactions involving RNA (reverse transcription, RT-PCR). Briefly, a small volume of whole, anti-coagulated blood is loaded onto a microfluidics chip, for example chips available from Caliper (Mountain View, CA) or Nanogen (San Diego, CA.) A microfluidics chip may contain channels and reservoirs in which cells are moved and reactions are performed. Mechanical, electrical, magnetic, gravitational, centrifugal or other forces are used to move the cells and to expose them to reagents. For example, cells of whole blood are moved into a chamber containing hypotonic saline, which results in selective lysis of red blood cells after a 20-minute incubation. Next, the remaining cells (leukocytes) are moved into a wash chamber and finally, moved into a chamber containing a lysis buffer such as guanidine isothyocyanate. The leukocyte cell lysate is further processed for RNA isolation in the chip, or is then removed for further processing, for example, RNA extraction by standard methods. Alternatively, the microfluidics chip is a circular disk containing ficoll or another density reagent. The blood sample is injected into the center of the disc, the disc is rotated at a speed that generates a centrifugal force appropriate for density gradient separation of mononuclear cells, and the separated mononuclear cells are then harvested for further analysis or processing.

It is understood that the methods of expression evaluation, above, although discussed in the context of discovery of diagnostic nucleotide sets, are also applicable for expression evaluation when using diagnostic nucleotide sets for, e.g. diagnosis of diseases, as further discussed below.

Evaluation of expression patterns

Expression patterns can be evaluated by qualitative and/or quantitative measures. Certain of the above described techniques for evaluating gene expression (as RNA or protein products) yield data that are predominantly qualitative in nature. That is, the methods detect differences in expression that classify expression into distinct modes without providing significant information regarding quantitative aspects of expression. For example, a technique can be described as a qualitative technique if it detects the presence or absence of expression of an candidate nucleotide sequence, i.e., an on/off pattern of expression. Alternatively, a qualitative technique measures the presence (and/or absence) of different alleles, or variants, of a gene product.

In contrast, some methods provide data that characterizes expression in a quantitative manner. That is, the methods relate expression on a numerical scale, e.g., a scale of 0-5, a scale of 1-10, a scale of + - +++, from grade 1 to grade 5, a grade from a to z, or the like. It will be understood that the numerical, and symbolic examples provided are arbitrary, and that any graduated scale (or any symbolic representation of a graduated scale) can be employed in the context of the present invention to describe quantitative differences in nucleotide sequence expression. Typically, such methods yield information corresponding to a relative increase or decrease in expression.

Any method that yields either quantitative or qualitative expression data is suitable for evaluating expression of candidate nucleotide sequence in a subject sample of leukocytes. In some cases, e.g., when multiple methods are employed to determine expression patterns for a plurality of candidate nucleotide sequences, the recovered data, e.g., the expression profile, for the nucleotide sequences is a combination of quantitative and qualitative data.

In some applications, expression of the plurality of candidate nucleotide sequences is evaluated sequentially. This is typically the case for methods that can be characterized as low- to moderate-throughput. In contrast, as the throughput of the elected assay increases, expression for the plurality of candidate nucleotide sequences in a sample or multiple samples of leukocytes, is assayed simultaneously. Again, the methods (and throughput) are largely determined by the individual practitioner, although, typically, it is preferable to employ methods that permit rapid, e.g. automated or partially automated, preparation and detection, on a scale that is time-efficient and cost-effective.

It is understood that the preceding discussion, while directed at the assessment of expression of the members of candidate libraries, is also applies to the assessment of the expression of members of diagnostic nucleotide sets, as further discussed below.

Genotyping

In addition to, or in conjunction with the correlation of expression profiles and clinical data, it is often desirable to correlate expression patterns with the subject's genotype at one or more genetic loci. The selected loci can be, for example, chromosomal loci corresponding to one or more member of the candidate library, polymorphic alleles for marker loci, or alternative disease related loci (not contributing to the candidate library) known to be, or putatively associated with, a disease (or disease criterion). Indeed, it will be appreciated, that where a (polymorphic) allele at a locus is linked to a disease (or to a predisposition to a disease), the presence of the allele can itself be a disease criterion.

Numerous well known methods exist for evaluating the genotype of an individual, including southern analysis, restriction fragment length polymorphism (RFLP) analysis, polymerase chain reaction (PCR), amplification length polymorphism (AFLP) analysis, single stranded conformation polymorphism (SSCP) analysis, single nucleotide polymorphism (SNP) analysis (e.g., via PCR, Taqman or molecular beacons), among many other useful methods. Many such procedures are readily adaptable to high throughput and/or automated (or semi-automated) sample preparation and analysis methods. Most, can be performed on nucleic acid samples recovered via simple procedures from the same sample of leukocytes as yielded the material for expression profiling. Exemplary techniques are described in, e.g., Sambrook, and Ausubel, *supra*.

Identification of the diagnostic nucleotide sets of the invention

Identification of diagnostic nucleotide sets and disease specific target nucleotide sequence proceeds by correlating the leukocyte expression profiles with data regarding the subject's health status to produce a data set designated a "molecular signature." Examples of data regarding a patient's health status, also termed "disease criteria(ion)", is described below and in the Section titled "selected diseases," below. Methods useful for correlation analysis are further described elsewhere in the specification.

Generally, relevant data regarding the subject's health status includes retrospective or prospective health data, e.g., in the form of the subject's medical history, as provided by the subject, physician or third party, such as, medical diagnoses, laboratory test results, diagnostic test results, clinical events, or medication lists, as further described below. Such data may include information regarding a patient's response to treatment and/or a particular medication and data regarding the presence of previously characterized "risk factors." For example, cigarette smoking and obesity are

previously identified risk factors for heart disease. Further examples of health status information, including diseases and disease criteria, is described in the section titled Selected diseases, below.

Typically, the data describes prior events and evaluations (i.e., retrospective data). However, it is envisioned that data collected subsequent to the sampling (i.e., prospective data) can also be correlated with the expression profile. The tissue sampled, e.g., peripheral blood, bronchial lavage, etc., can be obtained at one or more multiple time points and subject data is considered retrospective or prospective with respect to the time of sample procurement.

Data collected at multiple time points, called "longitudinal data", is often useful, and thus, the invention encompasses the analysis of patient data collected from the same patient at different time points. Analysis of paired samples, such as samples from a patient at different time, allows identification of differences that are specifically related to the disease state since the genetic variability specific to the patient is controlled for by the comparison. Additionally, other variables that exist between patients may be controlled for in this way, for example, the presence or absence of inflammatory diseases (e.g., rheumatoid arthritis) the use of medications that may effect leukocyte gene expression, the presence or absence of co-morbid conditions, etc. Methods for analysis of paired samples are further described below. Moreover, the analysis of a pattern of expression profiles (generated by collecting multiple expression profiles) provides information relating to changes in expression level over time, and may permit the determination of a rate of change, a trajectory, or an expression curve. Two longitudinal samples may provide information on the change in expression of a gene over time, while three longitudinal samples may be necessary to determine the "trajectory" of expression of a gene. Such information may be relevant to the diagnosis of a disease. For example, the expression of a gene may vary from individual to individual, but a clinical event, for example , a heart attack, may cause the level of expression to double in each patient. In this example, clinically interesting information is gleaned from the change in expression level, as opposed to the absolute level of expression in each individual.

When a single patient sample is obtained, it may still be desirable to compare the expression profile of that sample to some reference expression profile. In this case, one can determine the change of expression between the patient's sample and a reference expression profile that is appropriate for that patient and the medical condition in question. For example, a reference expression profile can be determined for all patients without the disease criterion in question who have similar characteristics, such as age, sex, race, diagnoses etc.

Generally, small sample sizes of 20-100 samples are used to identify a diagnostic nucleotide set. Larger sample sizes are generally necessary to validate the diagnostic nucleotide set for use in large and varied patient populations, as further described below. For example, extension of gene expression correlations to varied ethnic groups, demographic groups, nations, peoples or races may require expression correlation experiments on the population of interest.

Expression Reference Standards

Expression profiles derived from a patient (i.e., subjects diagnosed with, or exhibiting symptoms of, or exhibiting a disease criterion, or under a doctor's care for a disease) sample are compared to a control or standard expression RNA to facilitate comparison of expression profiles (e.g.

of a set of candidate nucleotide sequences) from a group of patients relative to each other (i.e., from one patient in the group to other patients in the group, or to patients in another group).

The reference RNA used should have desirable features of low cost and simplicity of production on a large scale. Additionally, the reference RNA should contain measurable amounts of as many of the genes of the candidate library as possible.

For example, in one approach to identifying diagnostic nucleotide sets, expression profiles derived from patient samples are compared to a expression reference "standard." Standard expression reference can be, for example, RNA derived from resting cultured leukocytes or commercially available reference RNA, such as Universal reference RNA from Stratagene. *See* Nature, V406, 8-17-00, p. 747-752. Use of an expression reference standard is particularly useful when the expression of large numbers of nucleotide sequences is assayed, e.g. in an array, and in certain other applications, e.g. qualitative PCR, RT-PCR, etc., where it is desirable to compare a sample profile to a standard profile, and/or when large numbers of expression profiles, e.g. a patient population, are to be compared. Generally, an expression reference standard should be available in large quantities, should be a good substrate for amplification and labeling reactions, and should be capable of detecting a large percentage of candidate nucleic acids using suitable expression profiling technology.

Alternatively, or in addition, the expression profile derived from a patient sample is compared with the expression of an internal reference control gene, for example, β-actin or CD4. The relative expression of the profiled genes and the internal reference control gene (from the same individual) is obtained. An internal reference control may also be used with a reference RNA. For example, an expression profile for "gene 1" and the gene encoding CD4 can be determined in a patient sample and in a reference RNA. The expression of each gene can be expressed as the "relative" ratio of expression the gene in the patient sample compared with expression of the gene in the reference RNA. The expression ratio (sample/reference) for gene 1 may be divided by the expression ration for CD4 (sample/reference) and thus the relative expression of gene 1 to CD4 is obtained.

The invention also provides a buffy coat control RNA useful for expression profiling, and a method of using control RNA produced from a population of buffy coat cells, the white blood cell layer derived from the centrifugation of whole blood. Buffy coat contains all white blood cells, including granulocytes, mononuclear cells and platelets. The invention also provides a method of preparing control RNA from buffy coat cells for use in expression profile analysis of leukocytes. Buffy coat fractions are obtained, e.g. from a blood bank or directly from individuals, preferably from a large number of individuals such that bias from individual samples is avoided and so that the RNA sample represents an average expression of a healthy population. Buffy coat fractions from about 50 or about 100, or more individuals are preferred. 10 ml buffy coat from each individual is used. Buffy coat samples are treated with an erthythrocyte lysis buffer, so that erthythrocytes are selectively removed. The leukocytes of the buffy coat layer are collected by centrifugation. Alternatively, the buffy cell sample can be further enriched for a particular leukocyte sub-populations, e.g. mononuclear cells, T-lymphocytes, etc. To enrich for mononuclear cells, the buffy cell pellet, above, is diluted in PBS (phosphate buffered saline) and loaded onto a non-polystyrene tube containing a polysucrose and sodium diatrizoate solution adjusted to a density of 1.077+/-0.001 g/ml. To enrich for T-lymphocytes,

45 ml of whole blood is treated with RosetteSep (Stem Cell Technologies), and incubated at room temperature for 20 minutes. The mixture is diluted with an equal volume of PBS plus 2% FBS and mixed by inversion. 30 ml of diluted mixture is layered on top of 15 ml DML medium (Stem Cell Technologies). The tube is centrifuged at 1200 x g, and the enriched cell layer at the plasma : medium interface is removed, washed with PBS + 2% FBS, and cells collected by centrifugation at 1200 x g. The cell pellet is treated with 5 ml of erythrocyte lysis buffer (EL buffer, Qiagen) for 10 minutes on ice, and enriched T-lymphoctes are collected by centrifugation.

In addition or alternatively, the buffy cells (whole buffy coat or sub-population, e.g. mononuclear fraction) can be cultured *in vitro* and subjected to stimulation with cytokines or activating chemicals such as phorbol esters or ionomycin. Such stimuli may increase expression of nucleotide sequences that are expressed in activated immune cells and might be of interest for leukocyte expression profiling experiments.

Following sub-population selection and/or further treatment, e.g. stimulation as described above, RNA is prepared using standard methods. For example, cells are pelleted and lysed with a phenol/guanidinium thiocyanate and RNA is prepared. RNA can also be isolated using a silica gel-based purification column or the column method can be used on RNA isolated by the phenol/guanidinium thiocyanate method. RNA from individual buffy coat samples can be pooled during this process, so that the resulting reference RNA represents the RNA of many individuals and individual bias is minimized or eliminated. In addition, a new batch of buffy coat reference RNA can be directly compared to the last batch to ensure similar expression pattern from one batch to another, using methods of collecting and comparing expression profiles described above/below. One or more expression reference controls are used in an experiment. For example, RNA derived from one or more of the following sources can be used as controls for an experiment: stimulated or unstimulated whole buffy coat, stimulated or unstimulated peripheral mononuclear cells, or stimulated or unstimulated T-lymphocytes.

Alternatively, the expression reference standard can be derived from any subject or class of subjects including healthy subjects or subjects diagnosed with the same or a different disease or disease criterion. Expression profiles from subjects in two distinct classes are compared to determine which subset of nucleotide sequences in the candidate library best distinguish between the two subject classes, as further discussed below. It will be appreciated that in the present context, the term "distinct classes" is relevant to at least one distinguishable criterion relevant to a disease of interest, a "disease criterion." The classes can, of course, demonstrate significant overlap (or identity) with respect to other disease criteria, or with respect to disease diagnoses, prognoses, or the like. The mode of discovery involves, e.g., comparing the molecular signature of different subject classes to each other (such as patient to control, patients with a first diagnosis to patients with a second diagnosis, etc.) or by comparing the molecular signatures of a single individual taken at different time points. The invention can be applied to a broad range of diseases, disease criteria, conditions and other clinical and/or epidemiological questions, as further discussed above/below.

It is appreciated that while the present discussion pertains to the use of expression reference controls while identifying diagnostic nucleotide sets, expression reference controls are also useful

during use of diagnostic nucleotide sets, e.g. use of a diagnostic nucleotide set for diagnosis of a disease, as further described below.

Analysis of expression profiles

In order to facilitate ready access, e.g., for comparison, review, recovery, and/or modification, the molecular signatures/expression profiles are typically recorded in a database. Most typically, the database is a relational database accessible by a computational device, although other formats, e.g., manually accessible indexed files of expression profiles as photographs, analogue or digital imaging readouts, spreadsheets, etc. can be used. Further details regarding preferred embodiments are provided below. Regardless of whether the expression patterns initially recorded are analog or digital in nature and/or whether they represent quantitative or qualitative differences in expression, the expression patterns, expression profiles (collective expression patterns), and molecular signatures (correlated expression patterns) are stored digitally and accessed via a database. Typically, the database is compiled and maintained at a central facility, with access being available locally and/or remotely.

As additional samples are obtained, and their expression profiles determined and correlated with relevant subject data, the ensuing molecular signatures are likewise recorded in the database. However, rather than each subsequent addition being added in an essentially passive manner in which the data from one sample has little relation to data from a second (prior or subsequent) sample, the algorithms optionally additionally query additional samples against the existing database to further refine the association between a molecular signature and disease criterion. Furthermore, the data set comprising the one (or more) molecular signatures is optionally queried against an expanding set of additional or other disease criteria. The use of the database in integrated systems and web embodiments is further described below.

Analysis of expression profile data from arrays

Expression data is analyzed using methods well known in the art, including the software packages Imagene (Biodiscovery, Marina del Rey, CA), Feature Extraction Software (Agilent, Palo Alto, CA), and Scanalyze (Stanford University). In the discussion that follows, a "feature" refers to an individual spot of DNA on an array. Each gene may be represented by more than one feature. For example, hybridized microarrays are scanned and analyzed on an Axon Instruments scanner using GenePix 3.0 software (Axon Instruments, Union City, CA). The data extracted by GenePix is used for all downstream quality control and expression evaluation. The data is derived as follows. The data for all features flagged as "not found" by the software is removed from the dataset for individual hybridizations. The "not found" flag by GenePix indicates that the software was unable to discriminate the feature from the background. Each feature is examined to determine the value of its signal. The median pixel intensity of the background (B_n) is subtracted from the median pixel intensity of the feature (F_n) to produce the background-subtracted signal (hereinafter, "BGSS"). The BGSS is divided by the standard deviation of the background pixels to provide the signal-to-noise ratio (hereinafter, "S/N"). Features with a S/N of three or greater in both the Cy3 channel (corresponding to the sample RNA) and Cy5 channel (corresponding to the reference RNA) are used for further analysis (hereinafter denoted "useable features"). Alternatively, different S/Ns are used for selecting expression data for an analysis. For example, only expression data with signal to noise ratios > 3 might be used in an

analysis. Alternatively, features with S/N values < 3 may be flagged as such and included in the analysis. Such flagged data sets include more values and may allow one to discover expression markers that would be missed otherwise. However, such data sets may have a higher variablilty than filtered data, which may decrease significance of findings or performance of correlation statistics.

For each usable feature (i), the expression level (e) is expressed as the logarithm of the ratio (R) of the Background Subtracted Signal (hereinafter "BGSS") for the Cy3 (sample RNA) channel divided by the BGSS for the Cy5 channel (reference RNA). This "log ratio" value is used for comparison to other experiments.

$$R_i = \frac{BGSS_{sample}}{BGSS_{reference}} \tag{0.1}$$

$$e_i = \log r_i \tag{0.2}$$

Variation in signal across hybridizations may be caused by a number of factors affecting hybridization, DNA spotting, wash conditions, and labeling efficiency.

A single reference RNA may be used with all of the experimental RNAs, permitting multiple comparisons in addition to individual comparisons. By comparing sample RNAs to the same reference, the gene expression levels from each sample are compared across arrays, permitting the use of a consistent denominator for our experimental ratios.

Alternative methods of analyzing the data may involve 1) using the sample channel without normalization by the reference channel, 2) using an intensity-dependent normalization based on the reference which provides a greater correction when the signal in the reference channel is large, 3) using the data without background subtraction or subtracting an empirically derived function of the background intensity rather than the background itself.

Scaling

The data may be scaled (normalized) to control for labeling and hybridization variability within the experiment, using methods known in the art. Scaling is desirable because it facilitates the comparison of data between different experiments, patients, etc. Generally the BGSS are scaled to a factor such as the median, the mean, the trimmed mean, and percentile. Additional methods of scaling include: to scale between 0 and 1, to subtract the mean, or to subtract the median.

Scaling is also performed by comparison to expression patterns obtained using a common reference RNA, as described in greater detail above. As with other scaling methods, the reference RNA facilitates multiple comparisons of the expression data, e.g., between patients, between samples, etc. Use of a reference RNA provides a consistent denominator for experimental ratios.

In addition to the use of a reference RNA, individual expression levels may be adjusted to correct for differences in labeling efficiency between different hybridization experiments, allowing direct comparison between experiments with different overall signal intensities, for example. A scaling factor (a) may be used to adjust individual expression levels as follows. The median of the scaling

factor (a), for example, BGSS, is determined for the set of all features with a S/N greater than three. Next, the $BGSS_i$ (the BGSS for each feature "i") is divided by the median for all features (a), generating a scaled ratio. The scaled ration is used to determine the expression value for the feature (e_i), or the log ratio.

$$S_i = \frac{BGSS_i}{a} \tag{0.3}$$

$$e_i = \log\left(\frac{Cy3S_i}{Cy5S_i}\right) \tag{0.4}$$

In addition, or alternatively, control features are used to normalize the data for labeling and hybridization variability within the experiment. Control feature may be cDNA for genes from the plant, *Arabidopsis thaliana*, that are included when spotting the mini-array. Equal amounts of RNA complementary to control cDNAs are added to each of the samples before they were labeled. Using the signal from these control genes, a normalization constant (L) is determined according to the following formula:

$$L_j = \frac{\dfrac{\sum\limits_{i=1}^{N} BGSS_{j,i}}{N}}{\dfrac{\sum\limits_{j=1}^{K} \dfrac{\sum\limits_{i=1}^{N} BGSS_{j,i}}{N}}{K}}$$

where $BGSS_i$ is the signal for a specific feature, N is the number of $A.\ thaliana$ control features, K is the number of hybridizations, and L_j is the normalization constant for each individual hybridization.

Using the formula above, the mean for all control features of a particular hybridization and dye (e.g., Cy3) is calculated. The control feature means for all Cy3 hybridizations are averaged, and the control feature mean in one hybridization divided by the average of all hybridizations to generate a normalization constant for that particular Cy3 hybridization (L_j), which is used as a in equation (0.3). The same normalization steps may be performed for Cy3 and Cy5 values.

An alternative scaling method can also be used. The log of the ratio of Green/Red is determined for all features. The median log ratio value for all features is determined. The feature values are then scaled using the following formula: Log_Scaled_Feature_Ratio = Log_Feature_Ratio − Median_Log_Ratio.

Many additional methods for normalization exist and can be applied to the data. In one method, the average ratio of Cy3 BGSS / Cy5 BGSS is determined for all features on an array. This ratio is then scaled to some arbitrary number, such as 1 or some other number. The ratio for each probe is then multiplied by the scaling factor required to bring the average ratio to the chosen level. This is

performed for each array in an analysis. Alternatively, the ratios are normalized to the average ratio across all arrays in an analysis. Other methods of normalization include forcing the distribution of signal strengths of the various arrays into greater agreement by transforming them to match certain points (quartiles, or deciles, etc.) in a standard distribution, or in the most extreme case using the rank of the signal of each oligonucleotide relative to the other oligonucleotides on the array.

If multiple features are used per gene sequence or oligonucleotide, these repeats can be used to derive an average expression value for each gene. If some of the replicate features are of poor qualitay and don't meet requirements for analysis, the remaining features can be used to represent the gene or gene sequence.

Correlation analysis

Correlation analysis is performed to determine which array probes have expression behavior that best distinguishes or serves as markers for relevant groups of samples representing a particular clinical condition. Correlation analysis, or comparison among samples representing different disease criteria (e.g., clinical conditions), is performed using standard statistical methods. Numerous algorithms are useful for correlation analysis of expression data, and the selection of algorithms depends in part on the data analysis to be performed. For example, algorithms can be used to identify the single most informative gene with expression behavior that reliably classifies samples, or to identify all the genes useful to classify samples. Alternatively, algorithms can be applied that determine which set of 2 or more genes have collective expression behavior that accurately classifies samples. The use of multiple expression markers for diagnostics may overcome the variability in expression of a gene between individuals, or overcome the variability intrinsic to the assay. Multiple expression markers may include redundant markers (surrogates), in that two or more genes or probes may provide the same information with respect to diagnosis. This may occur, for example, when two or more genes or gene probes are coordinately expressed. For diagnostic application, it may be appropriate to utilize a gene and one or more of its surrogates in the assay. This redundancy may overcome failures (technical or biological) of a single marker to distinguish samples. Alternatively, one or more surrogates may have properties that make them more suitable for assay development, such as a higher baseline level of expression, better cell specificity, a higher fold change between sample groups or more specific sequence for the design of PCR primers or complimentary probes. It will be appreciated that while the discussion above pertains to the analysis of RNA expression profiles the discussion is equally applicable to the analysis of profiles of proteins or other molecular markers.

Prior to analysis, expression profile data may be formatted or prepared for analysis using methods known in the art. For example, often the log ratio of scaled expression data for every array probe is calculated using the following formula:

log (Cy 3 BGSS/ Cy5 BGSS), where Cy 3 signal corresponds to the expression of the gene in the clinical sample, and Cy5 signal corresponds to expression of the gene in the reference RNA.

Data may be further filtered depending on the specific analysis to be done as noted below. For example, filtering may be aimed at selecting only samples with expression above a certain level, or probes with variability above a certain level between sample sets.

The following non-limiting discussion consider several statistical methods known in the art. Briefly, the t-test and ANOVA are used to identify single genes with expression differences between or among populations, respectively. Multivariate methods are used to identify a set of two or more genes for which expression discriminates between two disease states more specifically than expression of any single gene.

t-test

The simplest measure of a difference between two groups is the Student's t test. See, e.g., Welsh et al. (2001) Proc Natl Acad Sci USA 98:1176-81 (demonstrating the use of an unpaired Student's t-test for the discovery of differential gene expression in ovarian cancer samples and control tissue samples). The t- test assumes equal variance and normally distributed data. This test identifies the probability that there is a difference in expression of a single gene between two groups of samples. The number of samples within each group that is required to achieve statistical significance is dependent upon the variation among the samples within each group. The standard formula for a t-test is:

$$t(e_i) = \frac{\bar{e}_{i,c} - \bar{e}_{i,t}}{\sqrt{(s_{i,c}^2/n_c) + (s_{i,t}^2/n_t)}}, \tag{0.5}$$

where $\bar{e}_i$ is the difference between the mean expression level of gene i in groups c and t, $s_{i,c}$ is the variance of gene x in group c and $s_{i,t}$ is the variance of gene x in group t. n_c and n_t are the numbers of samples in groups c and t.

The combination of the t statistic and the degrees of freedom [min(n_t, n_c)-1] provides a p value, the probability of rejecting the null hypothesis. A p-value of ≤ 0.01, signifying a 99 percent probability the mean expression levels are different between the two groups (a 1% chance that the mean expression levels are in fact not different and that the observed difference occurred by statistical chance), is often considered acceptable.

When performing tests on a large scale, for example, on a large dataset of about 8000 genes, a correction factor must be included to adjust for the number of individual tests being performed. The most common and simplest correction is the Bonferroni correction for multiple tests, which divides the p-value by the number of tests run. Using this test on an 8000 member dataset indicates that a p value of ≤ 0.00000125 is required to identify genes that are likely to be truly different between the two test conditions.

Significance analysis for microarrays (SAM)

Significance analysis for microarrays (SAM) (Tusher 2001) is a method through which genes with a correlation between their expression values and the response vector are statistically discovered and assigned a statistical significance. The ratio of false significant to significant genes is the False Discovery Rate (FDR). This means that for each threshold there are a set of genes which are called significant, and the FDR gives a confidence level for this claim. If a gene is called differentially

expressed between 2 classes by SAM, with a FDR of 5%, there is a 95% chance that the gene is actually differentially expressed between the classes. SAM takes intoaccount the variability and large number of variables of microarrays. SAM will identiy genes that are most globally differentially expressed between the classes. Thus, important genes for identifying and classifying outlier samples or patients may not be identified by SAM.

Non-Parametric Tests

Wilcoxon's signed ranks method is one example of a non-parametric test and is utilized for paired comparisons. See e.g., Sokal and Rohlf (1987) Introduction to Biostatistics 2nd edition, WH Freeman, New York. At least 6 pairs are necessary to apply this statistic. This test is useful for analysis of paired expression data (for example, a set of patients who have cardiac transplant biopsy on 2 occasions and have a grade 0 on one occasion and a grade 3A on another). The Fisher Exact Test with a threshold and the Mann-Whitney Test are other non-parametric tests that may be used.

ANOVA

Differences in gene expression across multiple related groups may be assessed using an Analysis of Variance (ANOVA), a method well known in the art (Michelson and Schofield, 1996).

Multivariate analysis

Many algorithms suitable for multivariate analysis are known in the art. Generally, a set of two or more genes for which expression discriminates between two disease states more specifically than expression of any single gene is identified by searching through the possible combinations of genes using a criterion for discrimination, for example the expression of gene X must increase from normal 300 percent, while the expression of genes Y and Z must decrease from normal by 75 percent. Ordinarily, the search starts with a single gene, then adds the next best fit at each step of the search. Alternatively, the search starts with all of the genes and genes that do not aid in the discrimination are eliminated step-wise.

Paired samples

Paired samples, or samples collected at different time-points from the same patient, are often useful, as described above. For example, use of paired samples permits the reduction of variation due to genetic variation among individuals. In addition, the use of paired samples has a statistical significance, in that data derived from paired samples can be calculated in a different manner that recognizes the reduced variability. For example, the formula for a t-test for paired samples is:

$$t(e_x) = \frac{\overline{D_{e_x}}}{\sqrt{\dfrac{\sum D^2 - (\sum D)^2/b}{b-1}}},$$
(0.5)

where D is the difference between each set of paired samples and b is the number of sample pairs. $\overline{D}$ is the mean of the differences between the members of the pairs. In this test, only the differences between the paired samples are considered, then grouped together (as opposed to taking all possible differences between groups, as would be the case with an ordinary t-test). Additional statistical tests useful with paired data, e.g., ANOVA and Wilcoxon's signed rank test, are discussed above.

Diagnostic classification

Once a discriminating set of genes is identified, the diagnostic classifier (a mathematical function that assigns samples to diagnostic categories based on expression data) is applied to unknown sample expression levels.

Methods that can be used for this analysis include the following non-limiting list:

CLEAVER is an algorithm used for classification of useful expression profile data. See Raychaudhuri et al. (2001) Trends Biotechnol 19:189-193. CLEAVER uses positive training samples (e.g., expression profiles from samples known to be derived from a particular patient or sample diagnostic category, disease or disease criteria), negative training samples (e.g., expression profiles from samples known not to be derived from a particular patient or sample diagnostic category, disease or disease criteria) and test samples (e.g., expression profiles obtained from a patient), and determines whether the test sample correlates with the particular disease or disease criteria, or does not correlate with a particular disease or disease criteria. CLEAVER also generates a list of the 20 most predictive genes for classification.

Artificial neural networks (hereinafter, "ANN") can be used to recognize patterns in complex data sets and can discover expression criteria that classify samples into more than 2 groups. The use of artificial neural networks for discovery of gene expression diagnostics for cancers using expression data generated by oligonucleotide expression microarrays is demonstrated by Khan et al. (2001) Nature Med. 7:673-9. Khan found that 96 genes provided 0% error rate in classification of the tumors. The most important of these genes for classification was then determined by measuring the sensitivity of the classification to a change in expression of each gene. Hierarchical clustering using the 96 genes results in correct grouping of the cancers into diagnostic categories.

Golub uses cDNA microarrays and a distinction calculation to identify genes with expression behavior that distinguishes myeloid and lymphoid leukemias. See Golub et al. (1999) Science 286:531-7. Self organizing maps were used for new class discovery. Cross validation was done with a "leave one out" analysis. 50 genes were identified as useful markers. This was reduced to as few as 10 genes with equivalent diagnostic accuracy.

Hierarchical and non-hierarchical clustering methods are also useful for identifying groups of genes that correlate with a subset of clinical samples such as with transplant rejection grade. Alizadeh used hierarchical clustering as the primary tool to distinguish different types of diffuse B-cell lymphomas based on gene expression profile data. See Alizadeh et al. (2000) Nature 403:503-11. Alizadeh used hierarchical clustering as the primary tool to distinguish different types of diffuse B-cell lymphomas based on gene expression profile data. A cDNA array carrying 17856 probes was used for these experiments, 96 samples were assessed on 128 arrays, and a set of 380 genes was identified as being useful for sample classification.

Perou demonstrates the use of hierarchical clustering for the molecular classification of breast tumor samples based on expression profile data. See Perou el al. (2000) Nature 406:747-52. In this work, a cDNA array carrying 8102 gene probes was used. 1753 of these genes were found to have high variation between breast tumors and were used for the analysis.

Hastie describes the use of gene shaving for discovery of expression markers. Hastie et al. (2000) Genome Biol. 1(2):RESEARCH 0003.1-0003.21. The gene shaving algorithm identifies sets of genes with similar or coherent expression patterns, but large variation across conditions (RNA samples, sample classes, patient classes). In this manner, genes with a tight expression pattern within a transplant rejection grade, but also with high variability across rejection grades are grouped together. The algorithm takes advantage of both characteristics in one grouping step. For example, gene shaving can identify useful marker genes with co-regulated expression. Sets of useful marker genes can be reduced to a smaller set, with each gene providing some non-redundant value in classification. This algorithm was used on the data set described in Alizadeh et al., supra, and the set of 380 informative gene markers was reduced to 234.

Supervised harvesting of expression trees (Hastie 2001) identifies genes or clusters that best distinguish one class from all the others on the data set. The method is used to identify the genes/clusters that can best separate one class versus all the others for datasets that include two or more classes or all classes from each other. This algorithm can be used for discovery or testing of a diagnostic gene set.

CART is a decision tree classification algorithm (Breiman 1984). From gene expression and or other data, CART can develop a decision tree for the classification of samples. Each node on the decision tree involves a query about the expression level of one or more genes or variables. Samples that are above the threshold go down one branch of the decision tree and samples that are not go down the other branch. See example 4 for further description of its use in classification analysis and examples of its usefulness in discovering and implementing a diagnostic gene set. CART identifies surrogates for each splitter (genes that are the next best substitute for a useful gene in classification.

Multiple Additive Regression Trees (Friedman, JH 1999, MART) is similar to CART in that it is a classification algorithm that builds decision trees to distinguish groups. MART builds numerous trees for any classification problem and the resulting model involves a combination of the multiple trees. MART can select variables as it build models and thus can be used on large data sets, such as those derived from an 8000 gene microarray. Because MART uses a combination of many trees and does not take too much information from any one tree, it resists over training. MART identifies a set of genes and an algorithm for their use as a classifier.

A Nearest Shrunken Centroids Classifier can be applied to microarray or other data sets by the methods described by Tibshirani et al. 2002. This algorithms also identified gene sets for classification and determines their 10 fold cross validation error rates for each class of samples. The algorithm determines the error rates for models of any size, from one gene to all genes in the set. The error rates for either or both sample classes can are minimized when a particular number of genes are used. When this gene number is determined, the algorithm associated with the selected genes can be identified and employed as a classifier on prospective sample.

Once a set of genes and expression criteria for those genes have been established for classification, cross validation is done. There are many approaches, including a 10 fold cross validation analysis in which 10% of the training samples are left out of the analysis and the classification algorithm is built with the remaining 90%. The 10% are then used as a test set for the

algorithm. The process is repeated 10 times with 10% of the samples being left out as a test set each time. Through this analysis, one can derive a cross validation error which helps estimate the robustness of the algorithm for use on prospective (test) samples.

Clinical data are gathered for every patient sample used for expression analysis. Clinical variables can be quantitative or non-quantitative. A clinical variable that is quantitiative can be used as a variable for significance or classification analysis. Non-quantitative clinical variables, such as the sex of the patient, can also be used in a significance analysis or classification analysis with some statistical tool. It is appreciated that the most useful diagnostic gene set for a condition may be optimal when considered along with one or more predictive clinical variables. Clinical data can also be used as supervising vectors for a correlation analysis. That is to say that the clinical data associated with each sample can be used to divide the samples into meaningful diagnostic categories for analysis. For example, samples can be divided into 2 or more groups based on the presence or absence of some diagnostic criterion (a). In addition, clinical data can be utilized to select patients for a correlation analysis or to exclude them based on some undesirable characteristic, such as an ongoing infection, a medicine or some other issue. Clincial data can also be used to assess the pre-test probability of an outcome. For example, patients who are female are much more likely to be diagnosed as having systemic lupus erythematosis than patients who are male.

Once a set of genes are identified that classify samples with acceptable accuracy. These genes are validated as a set using new samples that were not used to discover the gene set. These samples can be taken from frozen archieves from the discovery clinical study or can be taken from new patients prospectively. Validation using a "test set" of samples can be done using expression profiling of the gene set with microarrays or using real-time PCR for each gene on the test set samples. Alternatively, a different expression profiling technology can be used.

Immune Monitoring

Leukocyte gene expression can be used to monitor the immune system. Immune monitoring examines both the level of gene expression for a set of genes in a given cell type and for genes which are expressed in a cell type selective manner gene expression monitoring will also detect the presence or absence of new cell types, progenitor cells, differentiation of cells and the like. Gene expression patterns may be associated with activation or the resting state of cells of the immune system that are responsible for or responsive to a disease state. For example, in the process of transplant rejection, cells of the immune system are activated by the presence of the foreign tissue. Genes and gene sets that monitor and diagnose this process are providing a measure of the level and type of activation of the immune system. Genes and gene sets that are useful in monitoring the immune system may be useful for diagnosis and monitoring of all diseases that involve the immune system. Some examples are transplant rejection, rheumatoid arthritis, lupus, inflammatory bowel diseases, multiple sclerosis, HIV/AIDS, and viral, bacterial and fungal infection. All disorders and diseases disclosed herein are contemplated. Genes and gene sets that monitor immune activation are useful for monitoring response to immunosuppressive drug therapy, which is used to decrease immune activation. Genes are found to correlate with immune activation by correlation of expression patterns to the known presence of immune activation or quiescence in a sample as determined by some other test.

Selected Diseases

In principle, diagnostic nucleotide sets of the invention may be developed and applied to essentially any disease, or disease criterion, as long as at least one subset of nucleotide sequences is differentially expressed in samples derived from one or more individuals with a disease criteria or disease and one or more individuals without the disease criteria or disease, wherein the individual may be the same individual sampled at different points in time, or the individuals may be different individuals (or populations of individuals). For example, the subset of nucleotide sequences may be differentially expressed in the sampled tissues of subjects with the disease or disease criterion (e.g., a patient with a disease or disease criteria) as compared to subjects without the disease or disease criterion (e.g., patients without a disease (control patients)). Alternatively, or in addition, the subset of nucleotide sequence(s) may be differentially expressed in different samples taken from the same patient, e.g at different points in time, at different disease stages, before and after a treatment, in the presence or absence of a risk factor, etc.

Expression profiles corresponding to sets of nucleotide sequences that correlate not with a diagnosis, but rather with a particular aspect of a disease can also be used to identify the diagnostic nucleotide sets and disease specific target nucleotide sequences of the invention. For example, such an aspect, or disease criterion, can relate to a subject's medical or family history, e.g., childhood illness, cause of death of a parent or other relative, prior surgery or other intervention, medications, symptoms (including onset and/or duration of symptoms), etc. Alternatively, the disease criterion can relate to a diagnosis, e.g., hypertension, diabetes, atherosclerosis, or prognosis (e.g., prediction of future diagnoses, events or complications), e.g., acute myocardial infarction, restenosis following angioplasty, reperfusion injury, allograft rejection, rheumatoid arthritis or systemic lupus erythematosis disease activity or the like. In other cases, the disease criterion corresponds to a therapeutic outcome, e.g., transplant rejection, bypass surgery or response to a medication, restenosis after stent implantation, collateral vessel growth due to therapeutic angiogenesis therapy, decreased angina due to revascularization, resolution of symptoms associated with a myriad of therapies, and the like. Alternatively, the disease criteria corresponds with previously identified or classic risk factors and may correspond to prognosis or future disease diagnosis. As indicated above, a disease criterion can also correspond to genotype for one or more loci. Disease criteria (including patient data) may be collected (and compared) from the same patient at different points in time, from different patients, between patients with a disease (criterion) and patients respresenting a control population, etc. Longitudinal data, i.e., data collected at different time points from an individual (or group of individuals) may be used for comparisons of samples obtained from an individual (group of individuals) at different points in time, to permit identification of differences specifically related to the disease state, and to obtain information relating to the change in expression over time, including a rate of change or trajectory of expression over time. The usefulness of longitudinal data is further discussed in the section titled "Identification of diagnostic nucleotide sets of the invention".

It is further understood that diagnostic nucleotide sets may be developed for use in diagnosing conditions for which there is no present means of diagnosis. For example, in rheumatoid arthritis, joint destruction is often well under way before a patient experience symptoms of the condition. A

diagnostic nucleotide set may be developed that diagnoses rheumatic joint destruction at an earlier stage than would be possible using present means of diagnosis, which rely in part on the presentation of symptoms by a patient. Diagnostic nucleotide sets may also be developed to replace or augment current diagnostic procedures. For example, the use of a diagnostic nucleotide set to diagnose cardiac allograft rejection may replace the current diagnostic test, a graft biopsy.

It is understood that the following discussion of diseases is exemplary and non-limiting, and further that the general criteria discussed above, e.g. use of family medical history, are generally applicable to the specific diseases discussed below.

In addition to leukocytes, as described throughout, the general method is applicable to nucleotide sequences that are differentially expressed in any subject tissue or cell type, by the collection and assessment of samples of that tissue or cell type. However, in many cases, collection of such samples presents significant technical or medical problems given the current state of the art.

Organ transplant rejection and success

A frequent complication of organ transplantation is recognition of the transplanted organ as foreign by the immune system resulting in rejection. Diagnostic nucleotide sets can be identified and validated for monitoring organ transplant success, rejection and treatment. Medications currently exist that suppress the immune system, and thereby decrease the rate of and severity of rejection. However, these drugs also suppress the physiologic immune responses, leaving the patient susceptible to a wide variety of opportunistic infections and cancers. At present there is no easy, reliable way to diagnose transplant rejection. Organ biopsy is the preferred method, but this is expensive, painful and associated with significant risk and has inadequate sensitivity for focal rejection.

Diagnostic nucleotide sets of the present invention can be developed and validated for use as diagnostic tests for transplant rejection and success. It is appreciated that the methods of identifying diagnostic nucleotide sets are applicable to any organ transplant population. For example, diagnostic nucleotide sets are developed for cardiac allograft rejection and success.

In some cases, disease criteria correspond to acute stage rejection diagnosis based on organ biopsy and graded using the International Society for Heart and Lung Transplantation ("ISHLT") criteria. This grading system classifies endomyocardial biopsies on the histological level as Grade 0, 1A, 1B, 2, 3A, 3B, or 4. Grade 0 biopies have no evidence of rejection, while each successive grade has increased severity of leukocyte infiltration and/or damage to the graft myocardial cells. It is appreciated that there is variability in the Grading systems between medical centers and pathologists and between repeated readings of the same pathologist at different times. When using the biopsy grade as a disease criterion for leukocyte gene expression correlation analysis, it may be desirable to have a single pathologist read all biopsy slides or have multiple pathologists read all slides to determine the variablility in this disease criterion. It is also appreciated that cardiac biopsy, in part due to variability, is not 100% sensitive or 100% specific for diagnosing acute rejection. When using the cardiac biopsy grade as a disease criterion for the discovery of diagnostic gene sets, it may be desirable to divide patient samples into diagnostic categories based on the grades. Examples of such classes are those patients with: Grade 0 vs. Grades 1A-4, Grade 0 vs. Grades 1B-4, Grade 0 vs. Grades 2-4, Grade 0-1 vs. Grade 2-4, Grade 0-1 vs. Grade 3A-4, or Grade 0 vs. Grade 3A-4.

Other disease criteria correspond to the cardiac biopsy results and other criteria, such as the results of cardiac function testing by echocardiography, hemodynamics assessment by cardiac catheterization, CMV infection, weeks post transplant, medication regimen, demographics and/or results of other diagnostic tests.

Other disease criteria correspond to information from the patient's medical history and information regarding the organ donor. Alternatively, disease criteria include the presence or absence of cytomegalovirus (CMV) infection, Epstein-Barr virus (EBV) infection, allograft dysfunction measured by physiological tests of cardiac function (e.g., hemodynamic measurements from catheterization or echocardiograph data), and symptoms of other infections. Alternatively, disease criteria correspond to therapeutic outcome, e.g. graft failure, re-transplantation, death, hospitalization, need for intravenous immunosuppression, transplant vasculopathy, response to immunosuppressive medications, etc. Disease criteria may further correspond to a rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteroids, anti-T cell antibodies, or total lymphoid irradiation; a rejection with histologic grade 2 or higher; a rejection with histologic grade <2; the absence of histologic rejection and normal or unchanged allograft function (based on hemodynamic measurements from catheterization or on echocardiographic data); the presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on hemodynamic measurements from catheterization or on echocardiographic data).; documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection; specific graft biopsy rejection grades; rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen; rejection of mild to moderate severity with allograft dysfunction prompting plasmaphoresis or a diagnosis of "humoral" rejection; infections other than CMV, especially infection with Epstein Barr virus (EBV); lymphoproliferative disorder (also called post-transplant lymphoma); transplant vasculopathy diagnosed by increased intimal thickness on intravascular ultrasound (IVUS), angiography, or acute myocardial infarction; graft failure or retransplantation; and all cause mortality. Further specific examples of clinical data useful as disease criteria are provided in Example 3.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and monitoring of kidney allograft recipients. Disease criteria correspond to, e.g., results of biopsy analysis for kidney allograft rejection, serum creatine level, creatinine clearance, radiological imaging results for the kidney and urinalysis results. Another disease criterion corresponds to the need for hemodialysis, retransplantation, death or other renal replacement therapy. Diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of bone marrow transplant and liver transplantation pateints, respectively. Disease criteria for bone marrow transplant correspond to the diagnosis and monitoring of graft rejection and/or graft versus host disease, the recurrence of cancer, complications due to immunosuppression, hematologic abnormalities, infection, hospitalization and/or death. Disease criteria for liver transplant rejection include levels of serum markers for liver damage and liver function such as AST (aspartate aminotransferase), ALT (alanine aminotransferase), Alkaline phosphatase, GGT, (gamma-glutamyl transpeptidase) Bilirubin, Albumin and Prothrombin time. Further disease criteria correspond to hepatic encephalopathy, medication usage, ascites, graft failure,

retransplantation, hospitalization, complications of immunosuppression, results of diagnostic tests, results of radiological testing, death and histological rejection on graft biopsy. In addition, urine can be utilized for at the target tissue for profiling in renal transplant, while biliary and intestinal secretions and feces may be used favorably for hepatic or intestinal organ allograft rejection. Diagnostic nuclotide sets can also be discovered and developed for the diagnosis and monitoring of chronic renal allograft rejection .

In the case of renal allografts, gene expression markers may be identified that are secreted proteins. These proteins may be detected in the urine of allograft recipients using standard immunoassays. Proteins are more likely to be present in the urine if they are of low molecular weight. Lower molecular weight proteins are more likely to pass through the glomerular membrane and into the urine.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of xenograft recipients. This can include the transplantation of any organ from a non-human animal to a human or between non-human animals. Considerations for discovery and application of diagnostics and therapeutics and for disease criterion are substantially similar to those for allograft transplantation between humans.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and treatment of artificial organ recipients. This includes, but is not limited to mechanical circulatory support, artificial hearts, left ventricular assist devices, renal replacement therapies, organ prostheses and the like. Disease criteria are thrombosis (blood clots), infection, death, hospitalization, and worsening measures of organ function (e.g., hemodynamics, creatinine, liver function testing, renal function testing, functional capacity).

In another example, diagnostic nucleotide sets are developed and validated for use in matching donor organs to appropriate recipients. Diagnostic gene set can be discovered that correlate with successful matching of donor organ to recipient. Disease criteria include graft failure, acute and chronic rejection, death, hospitalization, immunosuppressive drug use, and complications of immunosuppression. Gene sets may be assayed from the donor or recipient's peripheral blood, organ tissue or some other tissue.

In another example, diagnostic nucleotide sets are developed and validated for use in diagnosis and induction of patient immune tolerance (decrease rejection of an allograft by the host immune system). Disease criteria include rejection, assays of immune activation, need for immunosupression and all disease criteria noted above for transplantation of each organ.

Viral diseases

Diagnostic leukocyte nucleotide sets may be developed and validated for use in diagnosing viral disease, as well as diagnosing and monitoring transplant rejection. In another aspect, viral nucleotide sequences may be added to a leukocyte nucleotide set for use in diagnosis of viral diseases, as well as diagnosing and monitoring transplant rejection. Alternatively, viral nucleotide sets and leukocyte nucleotides sets may be used sequentially.

Epstein-Barr virus (EBV)

EBV causes a variety of diseases such as mononucleosis, B-cell lymphoma, and pharyngeal carcinoma. It infects mononuclear cells and circulating atypical lymphocytes are a common manifestation of infection. Peripheral leukocyte gene expression is altered by infection. Transplant recipients and patients who are immunosuppressed are at increased risk for EBV-associated lymphoma.

Diagnostic nucleotide sets may be developed and validated for use in diagnosis and monitoring of EBV, as well as diagnosing and monitoring transplant rejection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. Alternatively, EBV nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing EBV. Disease criteria correspond with diagnosis of EBV, and, in patients who are EBV-sero-positive, presence (or prospective occurrence) of EBV-related illnesses such as mononucleosis, and EBV-associated lymphoma. Diagnostic nucleotide sets are useful for diagnosis of EBV, and prediction of occurrence of EBV-related illnesses.

Cytomegalovirus (CMV)

Cytomegalovirus cause inflammation and disease in almost any tissue, particularly the colon, lung, bone marrow and retina, and is a very important cause of disease in immunosuppressed patients, e.g. transplant, cancer, AIDS. Many patients are infected with or have been exposed to CMV, but not all patients develop clinical disease from the virus. Also, CMV negative recipients of allografts that come from CMV positive donors are at high risk for CMV infection. As immunosuppressive drugs are developed and used, it is increasingly important to identify patients with current or impending clinical CMV disease, because the potential benefit of immunosuppressive therapy must be balanced with the increased rate of clinical CMV infection and disease that may result from the use of immunosuppression therapy. CMV may also play a role in the occurrence of atherosclerosis or restenosis after angioplasty. CMV expression also correlates to transplant rejection, and is useful in diagnosing and monitoring transplant rejection.

Diagnostic nucleotide sets are developed for use in diagnosis and monitoring of CMV infection or re-activation of CMV infection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, CMV nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing CMV. Disease criteria correspond to diagnosis of CMV (e.g., sero-positive state) and presence of clinically active CMV. Disease criteria may also correspond to prospective data, e.g. the likelihood that CMV will become clinically active or impending clinical CMV infection. Antiviral medications are available and diagnostic nucleotide sets can be used to select patients for early treatment, chronic suppression or prophylaxis of CMV activity.

Hepatitis B and C

These chronic viral infections affect about 1.25 and 2.7 million patients in the US, respectively. Many patients are infected, but suffer no clinical manifestations. Some patients with infection go on to suffer from chronic liver failure, cirrhosis and hepatic carcinoma.

Diagnostic nucleotide sets are developed for use in diagnosis and monitoring of HBV or HCV infection. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, viral nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing the virus and monitoring progression of liver disease. Disease criteria correspond to diagnosis of the virus (e.g.,

sero-positive state or other disease symptoms). Alternatively, disease criteria correspond to liver damage, e.g., elevated alkaline phosphatase, ALT, AST or evidence of ongoing hepatic damage on liver biopsy. Alternatively, disease criteria correspond to serum liver tests (AST, ALT, Alkaline Phosphatase, GGT, PT, bilirubin), liver biopsy, liver ultrasound, viral load by serum PCR, cirrhosis, hepatic cancer, need for hospitalization or listing for liver transplant. Diagnostic nucleotide sets are used to diagnose HBV and HCV, and to predict likelihood of disease progression. Antiviral therapeutic usage, such as Interferon gamma and Ribavirin, can also be disease criteria.

HIV

HIV infects T cells and certainly causes alterations in leukocyte expression. Diagnostic nucleotide sets are developed for diagnosis and monitoring of HIV. In one aspect, the diagnostic nucleotide set is a leukocyte nucleotide set. In another aspect, viral nucleotide sequences are added to a leukocyte nucleotide set, for use in diagnosing the virus. Disease criteria correspond to diagnosis of the virus (e.g., sero-positive state). In addition, disease criteria correspond to viral load, CD4 T cell counts, opportunistic infection, response to antiretroviral therapy, progression to AIDS, rate of progression and the occurrence of other HIV related outcomes (e.g., malignancy, CNS disturbance). Response to antiretrovirals may also be disease criteria.

Pharmacogenomics

Pharmocogenomics is the study of the individual propensity to respond to a particular drug therapy (combination of therapies). In this context, response can mean whether a particular drug will work on a particular patient, e.g. some patients respond to one drug but not to another drug. Response can also refer to the likelihood of successful treatment or the assessment of progress in treatment. Titration of drug therapy to a particular patient is also included in this description, e.g. different patients can respond to different doses of a given medication. This aspect may be important when drugs with side-effects or interactions with other drug therapies are contemplated.

Diagnostic nucleotide sets are developed and validated for use in assessing whether a patient will respond to a particular therapy and/or monitoring response of a patient to drug therapy(therapies). Disease criteria correspond to presence or absence of clinical symptoms or clinical endpoints, presence of side-effects or interaction with other drug(s). The diagnostic nucleotide set may further comprise nucleotide sequences that are targets of drug treatment or markers of active disease.

Validation and accuracy of diagnostic nucleotide sets

Prior to widespread application of the diagnostic probe sets of the invention the predictive value of the probe set is validated. When the diagnostic probe set is discovered by microarray based expression analysis, the differential expression of the member genes may be validated by a less variable and more quantitive and accurate technology such as real time PCR. In this type of experiment the amplification product is measured during the PCR reaction. This enables the researcher to observe the amplification before any reagent becomes rate limiting for amplification. In kinetic PCR the measurement is of C_T (threshold cycle) or C_P (crossing point). This measurement ($C_T=C_P$) is the point at which an amplification curve crosses a threshold fluorescence value. The threshold is set to a point within the area where all of the reactions were in their linear phase of amplification. When measuring

C_T, a lower C_T value is indicative of a higher amount of starting material since an earlier cycle number means the threshold was crossed more quickly.

Several fluorescence methodologies are available to measure amplification product in real-time PCR. Taqman (Applied BioSystems, Fosier City, CA) uses fluorescence resonance energy transfer (FRET) to inhibit signal from a probe until the probe is degraded by the sequence specific binding and Taq 3' exonuclease activity. Molecular Beacons (Stratagene, La Jolla, CA) also use FRET technology, whereby the fluorescence is measured when a hairpin structure is relaxed by the specific probe binding to the amplified DNA. The third commonly used chemistry is Sybr Green, a DNA-binding dye (Molecular Probes, Eugene, OR). The more amplified product that is produced, the higher the signal. The Sybr Green method is sensitive to non-specific amplification products, increasing the importance of primer design and selection. Other detection chemistries can also been used, such as ethedium bromide or other DNA-binding dyes and many modifications of the fluorescent dye/quencher dye Taqman chemistry, for example scorpions.

Real-time PCR validation can be done as described in Example 12.

Typically, the oligonucleotide sequence of each probe is confirmed, e.g. by DNA sequencing using an oligonucleotide-specific primer. Partial sequence obtained is generally sufficient to confirm the identity of the oligonucleotide probe. Alternatively, a complementary polynucleotide is fluorescently labeled and hybridized to the array, or to a different array containing a resynthesized version of the oligo nucleotide probe, and detection of the correct probe is confirmed.

Typically, validation is performed by statistically evaluating the accuracy of the correspondence between the molecular signature for a diagnostic probe set and a selected indicator. For example, the expression differential for a nucleotide sequence between two subject classes can be expressed as a simple ratio of relative expression. The expression of the nucleotide sequence in subjects with selected indicator can be compared to the expression of that nucleotide sequence in subjects without the indicator, as described in the following equations.

$\Sigma E_x ai/N = E_x A$ the average expression of nucleotide sequence x in the members of group A;

$\Sigma E_x bi/M = E_x B$ the average expression of nucleotide sequence x in the members of group B;

$E_x A/ ExB = \Delta E_x AB$ the average differential expression of nucleotide sequence x between groups A and B:

where Σ indicates a sum; Ex is the expression of nucleotide sequence x relative to a standard; ai are the individual members of group A, group A has N members; bi are the individual members of group B, group B has M members.

The expression of at least two nucleotide sequences, e.g., nucleotide sequence X and nucleotide sequence Y are measured relative to a standard in at least one subject of group A (e.g., with a disease) and group B (e.g., without the disease). Ideally, for purposes of validation the indicator is independent from (i.e., not assigned based upon) the expression pattern. Alternatively, a minimum threshold of gene expression for nucleotide sequences X and Y, relative to the standard, are designated for assignment to group A. For nucleotide sequence x, this threshold is designated ΔEx, and for nucleotide sequence y, the threshold is designated ΔEy.

The following formulas are used in the calculations below:

Sensitivity = (true positives/true positives + false negatives)

Specificity = (true negatives/true negatives + false positives)

If, for example, expression of nucleotide sequence x above a threshold: x > ΔEx, is observed for 80/100 subjects in group A and for 10/100 subjects in group B, the sensitivity of nucleotide sequence x for the assignment to group A, at the given expression threshold ΔEx, is 80%, and the specificity is 90%.

If the expression of nucleotide sequence y is > ΔEy in 80/100 subjects in group A, and in 10/100 subjects in group B, then, similarly the sensitivity of nucleotide sequence y for the assignment to group A at the given threshold ΔEy is 80% and the specificity is 90%. If in addition, 60 of the 80 subjects in group A that meet the expression threshold for nucleotide sequence y also meet the expression threshold ΔEx and that 5 of the 10 subjects in group B that meet the expression threshold for nucleotide sequence y also meet the expression threshold ΔEx, the sensitivity of the test (x>ΔEx and y>ΔEy)for assignment of subjects to group A is 60% and the specificity is 95%.

Alternatively, if the criteria for assignment to group A are change to: Expression of x > ΔEx or expression of y > ΔEy, the sensitivity approaches 100% and the specificity is 85%.

Clearly, the predictive accuracy of any diagnostic probe set is dependent on the minimum expression threshold selected. The expression of nucleotide sequence X (relative to a standard) is measured in subjects of groups A (with disease) and B (without disease). The minimum threshold of nucleotide sequence expression for x, required for assignment to group A is designated ΔEx 1.

If 90/100 patients in group A have expression of nucleotide sequence x > ΔEx 1 and 20/100 patients in group B have expression of nucleotide sequence x > ΔEx 1, then the sensitivity of the expression of nucleotide sequence x (using ΔEx 1 as a minimum expression threshold) for assignment of patients to group A will be 90% and the specificity will be 80%.

Altering the minimum expression threshold results in an alteration in the specificity and sensitivity of the nucleotide sequences in question. For example, if the minimum expression threshold of nucleotide sequence x for assignment of subjects to group A is lowered to ΔEx 2, such that 100/100 subjects in group A and 40/100 subjects in group B meet the threshold, then the sensitivity of the test for assignment of subjects to group A will be 100% and the specificity will be 60%.

Thus, for 2 nucleotide sequences X and Y: the expression of nucleotide sequence x and nucleotide sequence y (relative to a standard) are measured in subjects belonging to groups A (with disease) and B (without disease). Minimum thresholds of nucleotide sequence expression for nucleotide sequences X and Y (relative to common standards) are designated for assignment to group A. For nucleotide sequence x, this threshold is designated ΔEx1 and for nucleotide sequence y, this threshold is designated ΔEy1.

If in group A, 90/100 patients meet the minimum requirements of expression ΔEx1 and ΔEy1, and in group B, 10/100 subjects meet the minimum requirements of expression ΔEx1 and ΔEy1, then the sensitivity of the test for assignment of subjects to group A is 90% and the specificity is 90%.

Increasing the minimum expression thresholds for X and Y to ΔEx2 and ΔEy2, such that in group A, 70/100 subjects meet the minimum requirements of expression ΔEx2 and ΔEy2, and in group

B, 3/100 subjects meet the minimum requirements of expression ΔEx2 and ΔEy2. Now the sensitivity of the test for assignment of subjects to group A is 70% and the specificity is 97%.

If the criteria for assignment to group A is that the subject in question meets either threshold, ΔEx2 or ΔEy2, and it is found that 100/100 subjects in group A meet the criteria and 20/100 subjects in group B meet the criteria, then the sensitivity of the test for assignment to group A is 100% and the specificity is 80%.

Individual components of a diagnostic probe set each have a defined sensitivity and specificity for distinguishing between subject groups. Such individual nucleotide sequences can be employed in concert as a diagnostic probe set to increase the sensitivity and specificity of the evaluation. The database of molecular signatures is queried by algorithms to identify the set of nucleotide sequences (i.e., corresponding to members of the probe set) with the highest average differential expression between subject groups. Typically, as the number of nucleotide sequences in the diagnostic probe set increases, so does the predictive value, that is, the sensitivity and specificity of the probe set. When the probe sets are defined they may be used for diagnosis and patient monitoring as discussed below. The diagnostic sensitivity and specificity of the probe sets for the defined use can be determined for a given probe set with specified expression levels as demonstrated above. By altering the expression threshold required for the use of each nucleotide sequence as a diagnostic, the sensitivity and specificity of the probe set can be altered by the practitioner. For example, by lowering the magnitude of the expression differential threshold for each nucleotide sequence in the set, the sensitivity of the test will increase, but the specificity will decrease. As is apparent from the foregoing discussion, sensitivity and specificity are inversely related and the predictive accuracy of the probe set is continuous and dependent on the expression threshold set for each nucleotide sequence. Although sensitivity and specificity tend to have an inverse relationship when expression thresholds are altered, both parameters can be increased as nucleotide sequences with predictive value are added to the diagnostic nucleotide set. In addition a single or a few markers may not be reliable expression markers across a population of patients. This is because of the variability in expression and measurement of expression that exists between measurements, individuals and individuals over time. Inclusion of a large number of candidate nucleotide sequences or large numbers of nucleotide sequences in a diagnostic nucleotide set allows for this variability as not all nucleotide sequences need to meet a threshold for diagnosis. Generally, more markers are better than a single marker. If many markers are used to make a diagnosis, the likelihood that all expression markers will not meet some thresholds based upon random variability is low and thus the test will give fewer false negatives.

It is appreciated that the desired diagnostic sensitivity and specificity of the diagnostic nucleotide set may vary depending on the intended use of the set. For example, in certain uses, high specificity and high sensitivity are desired. For example, a diagnostic nucleotide set for predicting which patient population may experience side effects may require high sensitivity so as to avoid treating such patients. In other settings, high sensitivity is desired, while reduced specificity may be tolerated. For example, in the case of a beneficial treatment with few side effects, it may be important to identify as many patients as possible (high sensitivity) who will respond to the drug, and treatment of some patients who will not respond is tolerated. In other settings, high specificity is desired and

reduced sensitivity may be tolerated. For example, when identifying patients for an early-phase clinical trial, it is important to identify patients who may respond to the particular treatment. Lower sensitivity is tolerated in this setting as it merely results in reduced patients who enroll in the study or requires that more patients are screened for enrollment.

Methods of using diagnostic nucleotide sets.

The invention also provide methods of using the diagnostic nucleotide sets to: diagnose disease; assess severity of disease; predict future occurrence of disease; predict future complications of disease; determine disease prognosis; evaluate the patient's risk, or "stratify" a group of patients; assess response to current drug therapy; assess response to current non-pharmacological therapy; determine the most appropriate medication or treatment for the patient; predict whether a patient is likely to respond to a particular drug; and determine most appropriate additional diagnostic testing for the patient, among other clinically and epidemiologically relevant applications.

The nucleotide sets of the invention can be utilized for a variety of purposes by physicians, healthcare workers, hospitals, laboratories, patients, companies and other institutions. As indicated previously, essentially any disease, condition, or status for which at least one nucleotide sequence is differentially expressed in leukocyte populations (or sub-populations) can be evaluated, e.g., diagnosed, monitored, etc. using the diagnostic nucleotide sets and methods of the invention. In addition to assessing health status at an individual level, the diagnostic nucleotide sets of the present invention are suitable for evaluating subjects at a "population level," e.g., for epidemiological studies, or for population screening for a condition or disease.

Collection and preparation of sample

RNA, protein and/or DNA is prepared using methods well-known in the art, as further described herein. It is appreciated that subject samples collected for use in the methods of the invention are generally collected in a clinical setting, where delays may be introduced before RNA samples are prepared from the subject samples of whole blood, e.g. the blood sample may not be promptly delivered to the clinical lab for further processing. Further delay may be introduced in the clinical lab setting where multiple samples are generally being processed at any given time. For this reason, methods which feature lengthy incubations of intact leukocytes at room temperature are not preferred, because the expression profile of the leukocytes may change during this extended time period. For example, RNA can be isolated from whole blood using a phenol/guanidine isothiocyanate reagent or another direct whole-blood lysis method, as described in, e.g., U.S. Patent Nos. 5,346,994 and 4,843,155. This method may be less preferred under certain circumstances because the large majority of the RNA recovered from whole blood RNA extraction comes from erythrocytes since these cells outnumber leukocytes 1000:1. Care must be taken to ensure that the presence of erythrocyte RNA and protein does not introduce bias in the RNA expression profile data or lead to inadequate sensitivity or specificity of probes.

Alternatively, intact leukocytes may be collected from whole blood using a lysis buffer that selectively lyses erythrocytes, but not leukocytes, as described, e.g., in (U.S. Patent Nos. 5,973,137, and 6,020,186). Intact leukocytes are then collected by centrifugation, and leukocyte RNA is isolated using standard protocols, as described herein. However, this method does not allow isolation of sub-

populations of leukocytes, e.g. mononuclear cells, which may be desired. In addition, the expression profile may change during the lengthy incubation in lysis buffer, especially in a busy clinical lab where large numbers of samples are being prepared at any given time.

Alternatively, specific leukocyte cell types can be separated using density gradient reagents (Boyum, A, 1968.). For example, mononuclear cells may be separated from whole blood using density gradient centrifugation, as described, e.g., in U.S. Patents Nos. 4190535, 4350593, 4751001, 4818418, and 5053134. Blood is drawn directly into a tube containing an anticoagulant and a density reagent (such as Ficoll or Percoll). Centrifugation of this tube results in separation of blood into an erythrocyte and granulocyte layer, a mononuclear cell suspension, and a plasma layer. The mononuclear cell layer is easily removed and the cells can be collected by centrifugation, lysed, and frozen. Frozen samples are stable until RNA can be isolated. Density centrifugation, however, must be conducted at room temperature, and if processing is unduly lengthy, such as in a busy clinical lab, the expression profile may change.

Alternatively, cells can be separated using fluorescence activated cell sorting (FACS) or some other technique, which divides cells into subsets based on gene or protein expression. This may be desirable to enrich the sample for cells of interest, but it may also introduce cell manipulations and time delays, which result in alteration of gene expression profiles (Cantor et al. 1975; Galbraith et al. 1999).

The quality and quantity of each clinical RNA sample is desirably checked before amplification and labeling for array hybridization, using methods known in the art. For example, one microliter of each sample may be analyzed on a Bioanalyzer (Agilent 2100 Palo Alto, CA. USA) using an RNA 6000 nano LabChip (Caliper, Mountain View, CA. USA). Degraded RNA is identified by the reduction of the 28S to 18S ribosomal RNA ratio and/or the presence of large quantities of RNA in the 25-100 nucleotide range.

It is appreciated that the RNA sample for use with a diagnostic nucleotide set may be produced from the same or a different cell population, sub-population and/or cell type as used to identify the diagnostic nucleotide set. For example, a diagnostic nucleotide set identified using RNA extracted from mononuclear cells may be suitable for analysis of RNA extracted from whole blood or mononuclear cells, depending on the particular characteristics of the members of the diagnostic nucleotide set. Generally, diagnostic nucleotide sets must be tested and validated when used with RNA derived from a different cell population, sub-population or cell type than that used when obtaining the diagnostic gene set. Factors such as the cell-specific gene expression of diagnostic nucleotide set members, redundancy of the information provided by members of the diagnostic nucleotide set, expression level of the member of the diagnostic nucleotide set, and cell-specific alteration of expression of a member of the diagnostic nucleotide set will contribute to the usefullness of using a different RNA source than that used when identifying the members of the diagnostic nucleotide set. It is appreciated that it may be desirable to assay RNA derived from whole blood, obviating the need to isolate particular cell types from the blood.

Rapid method of RNA extraction suitable for production in a clinical setting of high quality RNA for expression profiling

In a clinical setting, obtaining high quality RNA preparations suitable for expression profiling, from a desired population of leukocytes poses certain technical challenges, including: the lack of capacity for rapid, high-throughput sample processing in the clinical setting, and the possibility that delay in processing (in a busy lab or in the clinical setting) may adversely affect RNA quality, e.g. by a permitting the expression profile of certain nucleotide sequences to shift. Also, use of toxic and expensive reagents, such as phenol, may be disfavored in the clinical setting due to the added expense associated with shipping and handling such reagents.

A useful method for RNA isolation for leukocyte expression profiling would allow the isolation of monocyte and lymphocyte RNA in a timely manner, while preserving the expression profiles of the cells, and allowing inexpensive production of reproducible high-quality RNA samples. Accordingly, the invention provides a method of adding inhibitor(s) of RNA transcription and/or inhibitor(s) of protein synthesis, such that the expression profile is "frozen" and RNA degradation is reduced. A desired leukocyte population or sub-population is then isolated, and the sample may be frozen or lysed before further processing to extract the RNA. Blood is drawn from subject population and exposed to ActinomycinD (to a final concentration of 10 ug/ml) to inhibit transcription, and cycloheximide (to a final concentration of 10 ug/ml) to inhibit protein synthesis. The inhibitor(s) can be injected into the blood collection tube in liquid form as soon as the blood is drawn, or the tube can be manufactured to contain either lyophilized inhibitors or inhibitors that are in solution with the anticoagulant. At this point, the blood sample can be stored at room temperature until the desired leukocyte population or sub-population is isolated, as described elsewhere. RNA is isolated using standard methods, e.g., as described above, or a cell pellet or extract can be frozen until further processing of RNA is convenient.

The invention also provides a method of using a low-temperature density gradient for separation of a desired leukocyte sample. In another embodiment, the invention provides the combination of use of a low-temperature density gradient and the use of transcriptional and/or protein synthesis inhibitor(s). A desired leukocyte population is separated using a density gradient solution for cell separation that maintains the required density and viscosity for cell separation at 0-4°C. Blood is drawn into a tube containing this solution and may be refrigerated before and during processing as the low temperatures slow cellular processes and minimize expression profile changes. Leukocytes are separated, and RNA is isolated using standard methods. Alternately, a cell pellet or extract is frozen until further processing of RNA is convenient. Care must be taken to avoid rewarming the sample during further processing steps.

Alternatively, the invention provides a method of using low-temperature density gradient separation, combined with the use of actinomycin A and cyclohexamide, as described above.

Assessing expression for diagnostics

Expression profiles for the set of diagnostic nucleotide sequences in a subject sample can be evaluated by any technique that determines the expression of each component nucleotide sequence. Methods suitable for expression analysis are known in the art, and numerous examples are discussed in

the Sections titled "Methods of obtaining expression data" and "high throughput expression Assays", above.

In many cases, evaluation of expression profiles is most efficiently, and cost effectively, performed by analyzing RNA expression. Alternatively, the proteins encoded by each component of the diagnostic nucleotide set are detected for diagnostic purposes by any technique capable of determining protein expression, e.g., as described above. Expression profiles can be assessed in subject leukocyte sample using the same or different techniques as those used to identify and validate the diagnostic nucleotide set. For example, a diagnostic nucleotide set identified as a subset of sequences on a cDNA microarray can be utilized for diagnostic (or prognostic, or monitoring, etc.) purposes on the same array from which they were identified. Alternatively, the diagnostic nucleotide sets for a given disease or condition can be organized onto a dedicated sub-array for the indicated purpose. It is important to note that if diagnostic nucleotide sets are discovered using one technology, e.g. RNA expression profiling, but applied as a diagnostic using another technology, e.g. protein expression profiling, the nucleotide sets must generally be validated for diagnostic purposes with the new technology. In addition, it is appreciated that diagnostic nucleotide sets that are developed for one use, e.g. to diagnose a particular disease, may later be found to be useful for a different application, e.g. to predict the likelihood that the particular disease will occur. Generally, the diagnostic nucleotide set will need to be validated for use in the second circumstance. As discussed herein, the sequence of diagnostic nucleotide set members may be amplified from RNA or cDNA using methods known in the art providing specific amplification of the nucleotide sequences.

General Protein Methods

Protein products of the nucleotide sequences of the invention may include proteins that represent functionally equivalent gene products. Such an equivalent gene product may contain deletions, additions or substitutions of amino acid residues within the amino acid sequence encoded by the nucleotide sequences described, above, but which result in a silent change, thus producing a functionally equivalent nucleotide sequence product. Amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved.

For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Functionally equivalent", as utilized herein, refers to a protein capable of exhibiting a substantially similar in vivo activity as the endogenous gene products encoded by the nucleotide described, above.

The gene products (protein products of the nucleotide sequences) may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing the gene polypeptides and peptides of the invention by expressing nucleic acid encoding nucleotide sequences are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing nucleotide sequence protein coding sequences and

appropriate transcriptional/translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques and in vivo recombination/genetic recombination. See, for example, the techniques described in Sambrook et al., 1989, supra, and Ausubel et al., 1989, supra. Alternatively, RNA capable of encoding nucleotide sequence protein sequences may be chemically synthesized using, for example, synthesizers. See, for example, the techniques described in "Oligonucleotide Synthesis", 1984, Gait, M. J. ed., IRL Press, Oxford, which is incorporated by reference herein in its entirety

A variety of host-expression vector systems may be utilized to express the nucleotide sequence coding sequences of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, exhibit the protein encoded by the nucleotide sequence of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing nucleotide sequence protein coding sequences; yeast (e.g. Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing the nucleotide sequence protein coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing the nucleotide sequence protein coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing nucleotide sequence protein coding sequences; or mammalian cell systems (e.g. COS, CHO, BHK, 293, 3T3) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5 K promoter).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the nucleotide sequence protein being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of antibodies or to screen peptide libraries, for example, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., 1983, EMBO J. 2:1791), in which the nucleotide sequence protein coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, 1985, Nucleic Acids Res. 13:3101-3109; Van Heeke & Schuster, 1989, J. Biol. Chem. 264:5503-5509); and the likes of pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target nucleotide sequence protein can be released from the GST moiety. Other systems useful in the invention include use of the FLAG epitope or the 6-HIS systems.

In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign nucleotide sequences. The virus grows in Spodoptera frugiperda cells. The nucleotide sequence coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter). Successful insertion of nucleotide sequence coding sequence will result in inactivation of the polyhedrin gene and production of non-occluded recombinant virus (i.e., virus lacking the proteinaceous coat coded for by the polyhedrin gene). These recombinant viruses are then used to infect Spodoptera frugiperda cells in which the inserted nucleotide sequence is expressed. (E.g., see Smith et al., 1983, J. Virol. 46: 584; Smith, U.S. Pat. No. 4,215,051).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the nucleotide sequence coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric nucleotide sequence may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing nucleotide sequence encoded protein in infected hosts. (E.g., See Logan & Shenk, 1984, Proc. Natl. Acad. Sci. USA 81:3655-3659). Specific initiation signals may also be required for efficient translation of inserted nucleotide sequence coding sequences. These signals include the ATG initiation codon and adjacent sequences. In cases where an entire nucleotide sequence, including its own initiation codon and adjacent sequences, is inserted into the appropriate expression vector, no additional translational control signals may be needed. However, in cases where only a portion of the nucleotide sequence coding sequence is inserted, exogenous translational control signals, including, perhaps, the ATG initiation codon, must be provided. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., 1987, Methods in Enzymol. 153:516-544).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the product of the nucleotide sequence in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERO, BHK, HeLa, COS, MDCK, 293, 3T3, WI38, etc.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the nucleotide sequence encoded protein may be

engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express nucleotide sequence encoded protein. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that affect the endogenous activity of the nucleotide sequence encoded protein.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler, et al., 1977, Cell 11:223), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, 1962, Proc. Natl. Acad. Sci. USA 48:2026), and adenine phosphoribosyltransferase (Lowy, et al., 1980, Cell 22:817) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for dhfr, which confers resistance to methotrexate (Wigler, et al., 1980, Natl. Acad. Sci. USA 77:3567; O'Hare, et al., 1981, Proc. Natl. Acad. Sci. USA 78:1527); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, 1981, Proc. Natl. Acad. Sci. USA 78:2072); neo, which confers resistance to the aminoglycoside G-418 (Colberre-Garapin, et al., 1981, J. Mol. Biol. 150:1); and hygro, which confers resistance to hygromycin (Santerre, et al., 1984, Gene 30:147) genes.

An alternative fusion protein system allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht, et al., 1991, Proc. Natl. Acad. Sci. USA 88: 8972-8976). In this system, the nucleotide sequence of interest is subcloned into a vaccinia recombination plasmid such that the nucleotide sequence's open reading frame is translationally fused to an amino-terminal tag consisting of six histidine residues. Extracts from cells infected with recombinant vaccinia virus are loaded onto Ni.sup.2 +-nitriloacetic acid-agarose columns and histidine-tagged proteins are selectively eluted with imidazole-containing buffers.

Where recombinant DNA technology is used to produce the protein encoded by the nucleotide sequence for such assay systems, it may be advantageous to engineer fusion proteins that can facilitate labeling, immobilization and/or detection.

Antibodies

Indirect labeling involves the use of a protein, such as a labeled antibody, which specifically binds to the protein encoded by the nucleotide sequence. Such antibodies include but are not limited to polyclonal, monoclonal, chimeric, single chain, Fab fragments and fragments produced by an Fab expression library.

The invention also provides for antibodies to the protein encoded by the nucleotide sequences. Described herein are methods for the production of antibodies capable of specifically recognizing one or more nucleotide sequence epitopes. Such antibodies may include, but are not limited to polyclonal antibodies, monoclonal antibodies (mAbs), humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab')2 fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-

Id) antibodies, and epitope-binding fragments of any of the above. Such antibodies may be used, for

example, in the detection of a nucleotide sequence in a biological sample, or, alternatively, as a method

for the inhibition of abnormal gene activity, for example, the inhibition of a disease target nucleotide

sequence, as further described below. Thus, such antibodies may be utilized as part of cardiovascular

or other disease treatment method, and/or may be used as part of diagnostic techniques whereby

patients may be tested for abnormal levels of nucleotide sequence encoded proteins, or for the presence

of abnormal forms of the such proteins.

For the production of antibodies to a nucleotide sequence, various host animals may be

immunized by injection with a protein encoded by the nucleotide sequence, or a portion thereof. Such

host animals may include but are not limited to rabbits, mice, and rats, to name but a few. Various

adjuvants may be used to increase the immunological response, depending on the host species,

including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum

hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil

emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as

BCG (bacille Calmette-Guerin) and Corynebacterium parvum.

Polyclonal antibodies are heterogeneous populations of antibody molecules derived from the

sera of animals immunized with an antigen, such as gene product, or an antigenic functional derivative

thereof. For the production of polyclonal antibodies, host animals such as those described above, may

be immunized by injection with gene product supplemented with adjuvants as also described above.

Monoclonal antibodies, which are homogeneous populations of antibodies to a particular

antigen, may be obtained by any technique which provides for the production of antibody molecules by

continuous cell lines in culture. These include, but are not limited to the hybridoma technique of Kohler

and Milstein, (1975, Nature 256:495-497; and U.S. Pat. No. 4,376,110), the human B-cell hybridoma

technique (Kosbor et al., 1983, Immunology Today 4:72; Cole et al., 1983, Proc. Natl. Acad. Sci. USA

80:2026-2030), and the EBV-hybridoma technique (Cole et al., 1985, Monoclonal Antibodies And

Cancer Therapy, Alan R. Liss, Inc., pp. 77-96). Such antibodies may be of any immunoglobulin class

including IgG, IgM, IgE, IgA, IgD and any subclass thereof. The hybridoma producing the mAb of this

invention may be cultivated in vitro or in vivo.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al.,

1984, Proc. Natl. Acad. Sci., 81:6851-6855; Neuberger et al., 1984, Nature, 312:604-608; Takeda et al.,

1985, Nature, 314:452-454) by splicing the genes from a mouse antibody molecule of appropriate

antigen specificity together with genes from a human antibody molecule of appropriate biological

activity can be used. A chimeric antibody is a molecule in which different portions are derived from

different animal species, such as those having a variable region derived from a murine mAb and a

human immunoglobulin constant region.

Alternatively, techniques described for the production of single chain antibodies (U.S. Pat.

No. 4,946,778; Bird, 1988, Science 242:423-426; Huston et al., 1988, Proc. Natl. Acad. Sci. USA

85:5879-5883; and Ward et al., 1989, Nature 334:544-546) can be adapted to produce nucleotide

sequence-single chain antibodies. Single chain antibodies are formed by linking the heavy and light

chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide.

Antibody fragments which recognize specific epitopes may be generated by known techniques For example, such fragments include but are not limited to: the F(ab')2 fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the F(ab')2 fragments. Alternatively, Fab expression libraries may be constructed (Huse et al., 1989, Science, 246:1275-1281) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

Disease specific target nucleotide sequences

The invention also provides disease specific target nucleotide sequences, and sets of disease specific target nucleotide sequences. The diagnostic nucleotide sets, subsets thereof, novel nucleotide sequences, and individual members of the diagnostic nucleotide sets identified as described above are also disease specific target nucleotide sequences. In particular, individual nucleotide sequences that are differentially regulated or have predictive value that is strongly correlated with a disease or disease criterion are especially favorable as disease specific target nucleotide sequences. Sets of genes that are co-regulated may also be identified as disease specific target nucleotide sets. Such nucleotide sequences and/or nucleotide sequence products are targets for modulation by a variety of agents and techniques. For example, disease specific target nucleotide sequences (or the products of such nucleotide sequences, or sets of disease specific target nucleotide sequences) can be inhibited or activated by, e.g., target specific monoclonal antibodies or small molecule inhibitors, or delivery of the nucleotide sequence or gene product of the nucleotide sequence to patients. Also, sets of genes can be inhibited or activated by a variety of agents and techniques. The specific usefulness of the target nucleotide sequence(s) depends on the subject groups from which they were discovered, and the disease or disease criterion with which they correlate.

Imaging

The invention also provides for imaging reagents. The differentially expressed leukocyte nucleotide sequences, diagnostic nucleotide sets, or portions thereof, and novel nucleotide sequences of the invention are nucleotide sequences expressed in cells with or without disease. Leukocytes expressing a nucleotide sequence(s) that is differentially expressed in a disease condition may localize within the body to sites that are of interest for imaging purposes. For example, a leukocyte expressing a nucleotide sequence(s) that are differentially expressed in an individual having atherosclerosis may localize or accumulate at the site of an atherosclerotic placque. Such leukocytes, when labeled, may provide a detection reagent for use in imaging regions of the body where labeled leukocyte accumulate or localize, for example, at the atherosclerotic plaque in the case of atherosclerosis. For example, leukocytes are collected from a subject, labeled in vitro, and reintroduced into a subject. Alternatively, the labeled reagent is introduced into the subject individual, and leukocyte labeling occurs within the patient.

Imaging agents that detect the imaging targets of the invention are produced by well-known molecular and immunological methods (for exemplary protocols, see, e.g., Ausubel, Berger, and Sambrook, as well as Harlow and Lane, supra).

For example, a full-length nucleic acid sequence, or alternatively, a gene fragment encoding an immunogenic peptide or polypeptide fragments, is cloned into a convenient expression vector, for

example, a vector including an in-frame epitope or substrate binding tag to facilitate subsequent purification. Protein is then expressed from the cloned cDNA sequence and used to generate antibodies, or other specific binding molecules, to one or more antigens of the imaging target protein. Alternatively, a natural or synthetic polypeptide (or peptide) or small molecule that specifically binds (or is specifically bound to) the expressed imaging target can be identified through well established techniques (*see*, e.g., Mendel et al. (2000) Anticancer Drug Des 15:29-41; Wilson (2000) Curr Med Chem 7:73-98; Hamby and Showwalter (1999) Pharmacol Ther 82:169-93; and Shimazawa et al. (1998) Curr Opin Struct Biol 8:451-8). The binding molecule, e.g., antibody, small molecule ligand, etc., is labeled with a contrast agent or other detectable label, e.g., gadolinium, iodine, or a gamma-emitting source. For in-vivo imaging of a disease process that involved leukocytes, the labeled antibody is infused into a subject, e.g., a human patient or animal subject, and a sufficient period of time is passed to permit binding of the antibody to target cells. The subject is then imaged with appropriate technology such as MRI (when the label is gadolinium) or with a gamma counter (when the label is a gamma emitter).

Identification of nucleotide sequence involved in leukocyte adhesion

The invention also encompasses a method of identifying nucleotide sequences involved in leukocyte adhesion. The interaction between the endothelial cell and leukocyte is a fundamental mechanism of all inflammatory disorders, including the diagnosis and prognosis of allograft rejection the diseases listed in Table 1. For example, the first visible abnormality in atherosclerosis is the adhesion to the endothelium and diapedesis of mononuclear cells (e.g., T-cell and monocyte). Insults to the endothelium (for example, cytokines, tobacco, diabetes, hypertension and many more) lead to endothelial cell activation. The endothelium then expresses adhesion molecules, which have counter receptors on mononuclear cells. Once the leukocyte receptors have bound the endothelial adhesion molecules, they stick to the endothelium, roll a short distance, stop and transmigrate across the endothelium. A similar set of events occurs in both acute and chronic inflammation. When the leukocyte binds the endothelial adhesion molecule, or to soluble cytokines secreted by endothelial or other cells, a program of gene expression is activated in the leukocyte. This program of expression leads to leukocyte rolling, firm adhesion and transmigration into the vessel wall or tissue parenchyma. Inhibition of this process is highly desirable goal in anti-inflammatory drug development. In addition, leukocyte nucleotide sequences and epithelial cell nucleotide sequences, that are differentially expressed during this process may be disease-specific target nucleotide sequences.

Human endothelial cells, e.g. derived from human coronary arteries, human aorta, human pulmonary artery, human umbilical vein or microvascular endothelial cells, are cultured as a confluent monolayer, using standard methods. Some of the endothelial cells are then exposed to cytokines or another activating stimuli such as oxidized LDL, hyperglycemia, shear stress, or hypoxia (Moser et al. 1992). Some endothelial cells are not exposed to such stimuli and serve as controls. For example, the endothelial cell monolayer is incubated with culture medium containing 5 U/ml of human recombinant IL-1alpha or 10 ng/ml TNF (tumor necrosis factor), for a period of minutes to overnight. The culture medium composition is changed or the flask is sealed to induce hypoxia. In addition, tissue culture plate is rotated to induce sheer stress.

Human T-cells and/or monocytes are cultured in tissue culture flasks or plates, with LGM-3 media from Clonetics. Cells are incubated at 37 degree C, 5% CO_2 and 95% humidity. These leukocytes are exposed to the activated or control endothelial layer by adding a suspension of leukocytes on to the endothelial cell monolayer. The endothelial cell monolayer is cultured on a tissue culture treated plate/ flask or on a microporous membrane. After a variable duration of exposures, the endothelial cells and leukocytes are harvested separately by treating all cells with trypsin and then sorting the endothelial cells from the leukocytes by magnetic affinity reagents to an endothelial cell specific marker such as PECAM-1 (Stem Cell Technologies). RNA is extracted from the isolated cells by standard techniques. Leukocyte RNA is labeled as described above, and hybridized to leukocyte candidate nucleotide library. Epithelial cell RNA is also labeled and hybridized to the leukocyte candidate nucleotide library. Alternatively, the epithelial cell RNA is hybridized to a epithelial cell candidate nucleotide library, prepared according to the methods described for leukocyte candidate libraries, above.

Hybridization to candidate nucleotide libraries will reveal nucleotide sequences that are up-regulated or down-regulated in leukocyte and/or epithelial cells undergoing adhesion. The differentially regulated nucleotide sequences are further characterized, e.g. by isolating and sequencing the full-length sequence, analysis of the DNA and predicted protein sequence, and functional characterization of the protein product of the nucleotide sequence, as described above. Further characterization may result in the identification of leukocyte adhesion specific target nucleotide sequences, which may be candidate targets for regulation of the inflammatory process. Small molecule or antibody inhibitors can be developed to inhibit the target nucleotide sequence function. Such inhibitors are tested for their ability to inhibit leukocyte adhesion in the in vitro test described above.

Integrated systems

Integrated systems for the collection and analysis of expression profiles, and molecular signatures, as well as for the compilation, storage and access of the databases of the invention, typically include a digital computer with software including an instruction set for sequence searching and analysis, and, optionally, high-throughput liquid control software, image analysis software, data interpretation software, a robotic control armature for transferring solutions from a source to a destination (such as a detection device) operably linked to the digital computer, an input device (e.g., a computer keyboard) for entering subject data to the digital computer, or to control analysis operations or high throughput sample transfer by the robotic control armature. Optionally, the integrated system further comprises an image scanner for digitizing label signals from labeled assay components, e.g., labeled nucleic acid hybridized to a candidate library microarray. The image scanner can interface with image analysis software to provide a measurement of the presence or intensity of the hybridized label, i.e., indicative of an on/off expression pattern or an increase or decrease in expression.

Readily available computational hardware resources using standard operating systems are fully adequate, e.g., a PC (Intel x86 or Pentium chip- compatible DOS,™ OS2,™ WINDOWS,™ WINDOWS NT,™ WINDOWS95,™ WINDOWS98,™ LINUX, or even Macintosh, Sun or PCs will suffice) for use in the integrated systems of the invention. Current art in software technology is similarly adequate (i.e., there are a multitude of mature programming languages and source code

suppliers) for design, e.g., of an upgradeable open-architecture object-oriented heuristic algorithm, or instruction set for expression analysis, as described herein. For example, software for aligning or otherwise manipulating ,molecular signatures can be constructed by one of skill using a standard programming language such as Visual basic, Fortran, Basic, Java, or the like, according to the methods herein.

Various methods and algorithms, including genetic algorithms and neural networks, can be used to perform the data collection, correlation, and storage functions, as well as other desirable functions, as described herein. In addition, digital or analog systems such as digital or analog computer systems can control a variety of other functions such as the display and/or control of input and output files.

For example, standard desktop applications such as word processing software (e.g., Corel WordPerfect™ or Microsoft Word™) and database software (e.g., spreadsheet software such as Corel Quattro Pro™, Microsoft Excel™, or database programs such as Microsoft Access™ or Paradox™) can be adapted to the present invention by inputting one or more character string corresponding, e.g., to an expression pattern or profile, subject medical or historical data, molecular signature, or the like, into the software which is loaded into the memory of a digital system, and carrying out the operations indicated in an instruction set, e.g., as exemplified in Figure 2. For example, systems can include the foregoing software having the appropriate character string information, e.g., used in conjunction with a user interface in conjunction with a standard operating system such as a Windows, Macintosh or LINUX system. For example, an instruction set for manipulating strings of characters, either by programming the required operations into the applications or with the required operations performed manually by a user (or both). For example, specialized sequence alignment programs such as PILEUP or BLAST can also be incorporated into the systems of the invention, e.g., for alignment of nucleic acids or proteins (or corresponding character strings).

Software for performing the statistical methods required for the invention, e.g., to determine correlations between expression profiles and subsets of members of the diagnostic nucleotide libraries, such as programmed embodiments of the statistical methods described above, are also included in the computer systems of the invention. Alternatively, programming elements for performing such methods as principle component analysis (PCA) or least squares analysis can also be included in the digital system to identify relationships between data. Exemplary software for such methods is provided by Partek, Inc., St. Peter, Mo; at the web site partek.com.

Any controller or computer optionally includes a monitor which can include, e.g., a flat panel display (e.g., active matrix liquid crystal display, liquid crystal display), a cathode ray tube ("CRT") display, or another display system which serves as a user interface, e.g., to output predictive data. Computer circuitry, including numerous integrated circuit chips, such as a microprocessor, memory, interface circuits, and the like, is often placed in a casing or box which optionally also includes a hard disk drive, a floppy disk drive, a high capacity removable drive such as a writeable CD-ROM, and other common peripheral elements.

Inputting devices such as a keyboard, mouse, or touch sensitive screen, optionally provide for input from a user and for user selection, e.g., of sequences or data sets to be compared or otherwise

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manipulated in the relevant computer system. The computer typically includes appropriate software for receiving user instructions, either in the form of user input into a set parameter or data fields (e.g., to input relevant subject data), or in the form of preprogrammed instructions, e.g., preprogrammed for a variety of different specific operations. The software then converts these instructions to appropriate language for instructing the system to carry out any desired operation.

The integrated system may also be embodied within the circuitry of an application specific integrated circuit (ASIC) or programmable logic device (PLD). In such a case, the invention is embodied in a computer readable descriptor language that can be used to create an ASIC or PLD. The integrated system can also be embodied within the circuitry or logic processors of a variety of other digital apparatus, such as PDAs, laptop computer systems, displays, image editing equipment, etc.

The digital system can comprise a learning component where expression profiles, and relevant subject data are compiled and monitored in conjunction with physical assays, and where correlations, e.g., molecular signatures with predictive value for a disease, are established or refined. Successful and unsuccessful combinations are optionally documented in a database to provide justification/preferences for user-base or digital system based selection of diagnostic nucleotide sets with high predictive accuracy for a specified disease or condition.

The integrated systems can also include an automated workstation. For example, such a workstation can prepare and analyze leukocyte RNA samples by performing a sequence of events including: preparing RNA from a human blood sample; labeling the RNA with an isotopic or non-isotopic label; hybridizing the labeled RNA to at least one array comprising all or part of the candidate library; and detecting the hybridization pattern. The hybridization pattern is digitized and recorded in the appropriate database.

Automated RNA preparation tool

The invention also includes an automated RNA preparation tool for the preparation of mononuclear cells from whole blood samples, and preparation of RNA from the mononuclear cells. In a preferred embodiment, the use of the RNA preparation tool is fully automated, so that the cell separation and RNA isolation would require no human manipulations. Full automation is advantageous because it minimizes delay, and standardizes sample preparation across different laboratories. This standardization increases the reproducibility of the results.

Figure 2 depicts the processes performed by the RNA preparation tool of the invention. A primary component of the device is a centrifuge (A). Tubes of whole blood containing a density gradient solution, transcription/translation inhibitors, and a gel barrier that separates erythrocytes from mononuclear cells and serum after centrifugation are placed in the centrifuge (B). The barrier is permeable to erythrocytes and granulocytes during centrifugation, but does not allow mononuclear cells to pass through (or the barrier substance has a density such that mononuclear cells remain above the level of the barrier during the centrifugation). After centrifugation, the erythrocytes and granulocytes are trapped beneath the barrier, facilitating isolation of the mononuclear cell and serum layers. A mechanical arm removes the tube and inverts it to mix the mononuclear cell layer and the serum (C). The arm next pours the supernatant into a fresh tube (D), while the erythrocytes and granulocytes remained below the barrier. Alternatively, a needle is used to aspirate the supernatant and

transfer it to a fresh tube. The mechanical arms of the device opens and closes lids, dispenses PBS to aid in the collection of the mononuclear cells by centrifugation, and moves the tubes in and out of the centrifuge. Following centrifugation, the supernatant is poured off or removed by a vacuum device (E), leaving an isolated mononuclear cell pellet. Purification of the RNA from the cells is performed automatically, with lysis buffer and other purification solutions (F) automatically dispensed and removed before and after centrifugation steps. The result is a purified RNA solution. In another embodiment, RNA isolation is performed using a column or filter method. In yet another embodiment, the invention includes an on-board homogenizer for use in cell lysis.

Other automated systems

Automated and/or semi-automated methods for solid and liquid phase high-throughput sample preparation and evaluation are available, and supported by commercially available devices. For example, robotic devices for preparation of nucleic acids from bacterial colonies, e.g., to facilitate production and characterization of the candidate library include, for example, an automated colony picker (e.g., the Q-bot, Genetix, U.K.) capable of identifying, sampling, and inoculating up to 10,000/4 hrs different clones into 96 well microtiter dishes. Alternatively, or in addition, robotic systems for liquid handling are available from a variety of sources, e.g., automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Beckman Coulter, Inc. (Fullerton, CA)) which mimic the manual operations performed by a scientist. Any of the above devices are suitable for use with the present invention, e.g., for high-throughput analysis of library components or subject leukocyte samples. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art.

High throughput screening systems that automate entire procedures, e.g., sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the relevant assay are commercially available. (*see, e.g.,* Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc. Fullerton, CA; Precision Systems, Inc., Natick, MA, *etc.*). These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. Similarly, arrays and array readers are available, e.g., from Affymetrix, PE Biosystems, and others.

The manufacturers of such systems provide detailed protocols the various high throughput. Thus, for example, Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

A variety of commercially available peripheral equipment, including, e.g., optical and fluorescent detectors, optical and fluorescent microscopes, plate readers, CCD arrays, phosphorimagers, scintillation counters, phototubes, photodiodes, and the like, and software is available for digitizing, storing and analyzing a digitized video or digitized optical or other assay results, e.g., using PC (Intel x86 or pentium chip- compatible DOS™, OS2™ WINDOWS™, WINDOWS NT™ or WINDOWS95™ based machines), MACINTOSH™, or UNIX based (*e.g.,* SUN™ work station) computers.

Embodiment in a web site.

The methods described above can be implemented in a localized or distributed computing environment. For example, if a localized computing environment is used, an array comprising a candidate nucleotide library, or diagnostic nucleotide set, is configured in proximity to a detector, which is, in turn, linked to a computational device equipped with user input and output features.

In a distributed environment, the methods can be implemented on a single computer with multiple processors or, alternatively, on multiple computers. The computers can be linked, e.g. through a shared bus, but more commonly, the computer(s) are nodes on a network. The network can be generalized or dedicated, at a local level or distributed over a wide geographic area. In certain embodiments, the computers are components of an intra-net or an internet.

The predictive data corresponding to subject molecular signatures (e.g., expression profiles, and related diagnostic, prognostic, or monitoring results) can be shared by a variety of parties. In particular, such information can be utilized by the subject, the subject's health care practitioner or provider, a company or other institution, or a scientist. An individual subject's data, a subset of the database or the entire database recorded in a computer readable medium can be accessed directly by a user by any method of communication, including, but not limited to, the internet. With appropriate computational devices, integrated systems, communications networks, users at remote locations, as well as users located in proximity to, e.g., at the same physical facility, the database can access the recorded information. Optionally, access to the database can be controlled using unique alphanumeric passwords that provide access to a subset of the data. Such provisions can be used, e.g., to ensure privacy, anonymity, etc.

Typically, a client (e.g., a patient, practitioner, provider, scientist, or the like) executes a Web browser and is linked to a server computer executing a Web server. The Web browser is, for example, a program such as IBM's Web Explorer, Internet explorer, NetScape or Mosaic, or the like. The Web server is typically, but not necessarily, a program such as IBM's HTTP Daemon or other WWW daemon (e.g., LINUX-based forms of the program). The client computer is bi-directionally coupled with the server computer over a line or via a wireless system. In turn, the server computer is bi-directionally coupled with a website (server hosting the website) providing access to software implementing the methods of this invention.

A user of a client connected to the Intranet or Internet may cause the client to request resources that are part of the web site(s) hosting the application(s) providing an implementation of the methods described herein. Server program(s) then process the request to return the specified resources (assuming they are currently available). A standard naming convention has been adopted, known as a Uniform Resource Locator ("URL"). This convention encompasses several types of location names, presently including subclasses such as Hypertext Transport Protocol ("http"), File Transport Protocol ("ftp"), gopher, and Wide Area Information Service ("WAIS"). When a resource is downloaded, it may include the URLs of additional resources. Thus, the user of the client can easily learn of the existence of new resources that he or she had not specifically requested.

Methods of implementing Intranet and/or Intranet embodiments of computational and/or data access processes are well known to those of skill in the art and are documented, e.g., in ACM Press, pp.

383-392; ISO-ANSI, Working Draft, "Information Technology-Database Language SQL", Jim
Melton, Editor, International Organization for Standardization and American National Standards
Institute, Jul. 1992; ISO Working Draft, "Database Language SQL-Part 2:Foundation
(SQL/Foundation)", CD9075-2:199.chi.SQL, Sep. 11, 1997; and Cluer et al. (1992) A General
Framework for the Optimization of Object-Oriented Queries, Proc SIGMOD International Conference
on Management of Data, San Diego, California, Jun. 2-5, 1992, SIGMOD Record, vol. 21, Issue 2,
Jun., 1992; Stonebraker, M., Editor;. Other resources are available, e.g., from Microsoft, IBM, Sun and
other software development companies.

        Using the tools described above, users of the reagents, methods and database as discovery or
diagnostic tools can query a centrally located database with expression and subject data. Each
submission of data adds to the sum of expression and subject information in the database. As data is
added, a new correlation statistical analysis is automatically run that incorporates the added clinical and
expression data. Accordingly, the predictive accuracy and the types of correlations of the recorded
molecular signatures increases as the database grows.

        For example, subjects, such as patients, can access the results of the expression analysis of
their leukocyte samples and any accrued knowledge regarding the likelihood of the patient's belonging
to any specified diagnostic (or prognostic, or monitoring, or risk group), i.e., their expression profiles,
and/or molecular signatures. Optionally, subjects can add to the predictive accuracy of the database by
providing additional information to the database regarding diagnoses, test results, clinical or other
related events that have occurred since the time of the expression profiling. Such information can be
provided to the database via any form of communication, including, but not limited to, the internet.
Such data can be used to continually define (and redefine) diagnostic groups. For example, if 1000
patients submit data regarding the occurrence of myocardial infarction over the 5 years since their
expression profiling, and 300 of these patients report that they have experienced a myocardial
infarction and 700 report that they have not, then the 300 patients define a new "group A." As the
algorithm is used to continually query and revise the database, a new diagnostic nucleotide set that
differentiates groups A and B (i.e., with and without myocardial infarction within a five year period) is
identified. This newly defined nucleotide set is then be used (in the manner described above) as a test
that predicts the occurrence of myocardial infarction over a five-year period. While submission
directly by the patient is exemplified above, any individual with access and authority to submit the
relevant data e.g., the patient's physician, a laboratory technician, a health care or study administrator,
or the like, can do so.

        As will be apparent from the above examples, transmission of information via the internet (or
via an intranet) is optionally bi-directional. That is, for example, data regarding expression profiles,
subject data, and the like are transmitted via a communication system to the database, while
information regarding molecular signatures, predictive analysis, and the like, are transmitted from the
database to the user. For example, using appropriate configurations of an integrated system including a
microarray comprising a diagnostic nucleotide set, a detector linked to a computational device can
directly transmit (locally or from a remote workstation at great distance, e.g., hundreds or thousands of
miles distant from the database) expression profiles and a corresponding individual identifier to a

central database for analysis according to the methods of the invention. According to, e.g., the algorithms described above, the individual identifier is assigned to one or more diagnostic (or prognostic, or monitoring, etc.) categories. The results of this classification are then relayed back, via, e.g., the same mode of communication, to a recipient at the same or different internet (or intranet) address.

   Kits

   The present invention is optionally provided to a user as a kit. Typically, a kit contains one or more diagnostic nucleotide sets of the invention. Alternatively, the kit contains the candidate nucleotide library of the invention. Most often, the kit contains a diagnostic nucleotide probe set, or other subset of a candidate library, e.g., as a cDNA or antibody microarray packaged in a suitable container. The kit may further comprise, one or more additional reagents, e.g., substrates, labels, primers, for labeling expression products, tubes and/or other accessories, reagents for collecting blood samples, buffers, e.g., erythrocyte lysis buffer, leukocyte lysis buffer, hybridization chambers, cover slips, etc., as well as a software package, e.g., including the statistical methods of the invention, e.g., as described above, and a password and/or account number for accessing the compiled database. The kit optionally further comprises an instruction set or user manual detailing preferred methods of using the diagnostic nucleotide sets in the methods of the invention. In one embodiment, the kit may include contents useful for the discovery of diagnostic nucleotide sets using microarrays. The kit may include sterile, endotoxin and RNAse free blood collection tubes. The kit may also include alcohol swabs, tourniquet, blood collection set, and/or PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA). The kit may also include cell lysis buffer. The kit may include RNA isolation kit, substrates for labeling of RNA (may vary for various expression profiling techniques). The kit may also include materials for fluorescence microarray expression profiling, including one or more of the following: reverse transcriptase and 10x RT buffer, T7(dT)24 primer (primer with T7 promoter at 5' end), DTT, deoxynucleotides, optionally 100mM each, RNAse inhibitor, second strand cDNA buffer, DNA polymerase, Rnase H, T7 RNA polymerase ribonucleotides, in vitro transcription buffer, and/or Cy3 and Cy5 labeled ribonucleotides. The kit may also include microarrays containing candidate gene libraries, cover slips for slides, and/or hybridization chambers. The kit may further include software package for identification of diagnostic gene set from data, that contains statistical methods, and/or allows alteration in desired sensitivity and specificity of gene set. The software may further facilitate access to and data analysis by centrally a located database server. The software may further include a password and account number to access central database server. In addition, the kit may include a kit user manual.

   In another embodiment, the kit may include contents useful for the application of diagnostic nucleotide sets using microarrays. The kit may include sterile, endotoxin and/or RNAse free blood collection tubes. The kit may also include, alcohol swabs, tourniquet, and/or a blood collection set. The kit may further include PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA), cell lysis buffer, and/or an RNA isolation kit. In addition, the kit may include substrates for labeling of RNA (may vary for various expression profiling techniques). For fluorescence microarray expression profiling, components may include reverse transcriptase and 10x

RT buffer, T7(dT)24 primer (primer with T7 promoter at 5' end), DTT, deoxynucleotides (optionally 100mM each), RNAse inhibitor, second strand cDNA buffer, DNA polymerase, Rnase H, T7 RNA polymerase, ribonucleotides, in vitro transcription buffer, and/or Cy3 and Cy5 labeled ribonucleotides. The kit may further include microarrays containing candidate gene libraries. The kit may also include cover slips for slides, and/or hybridization chambers. The kit may include a software package for identification of diagnostic gene set from data. The software package may contain statistical methods, allow alteration in desired sensitivity and specificity of gene set, and/or facilitate access to and data analysis by centrally located database server. The software package may include a password and account number to access central database server. In addition, the kit may include a kit user manual.

In another embodiment, the kit may include contents useful for the application of diagnostic nucleotide sets using real-time PCR. This kit may include terile, endotoxin and/or RNAse free blood collection tubes. The kit may further include alcohol swabs, tourniquet, and/or a blood collection set. The kit may also include PBS (phosphate buffer saline; needed when method of example 2 is used to derived mononuclear RNA). In addition, the kit may include cell lysis buffer and/or an RNA isolation kit. The kit may laso include substrates for real time RT-PCR, which may vary for various real-time PCR techniques, including poly dT primers, random hexamer primers, reverse Transcriptase and RT buffer, DTT, deoxynucleotides 100 mM, RNase H, primer pairs for diagnostic and control gene set, 10x PCR reaction buffer, and/or Taq DNA polymerase. The kit may also include fluorescent probes for diagnostic and control gene set (alternatively, fluorescent dye that binds to only double stranded DNA). The kit may further include reaction tubes with or without barcode for sample tracking, 96-well plates with barcode for sample identification, one barcode for entire set, or individual barcode per reaction tube in plate. The kit may also include a software package for identification of diagnostic gene set from data, and /or statistical methods. The software package may allow alteration in desired sensitivity and specificity of gene set, and/or facilitate access to and data analysis by centrally located database server. The kit may include a password and account number to access central database server. Finally, the kit may include a kit user manual.

This invention will be better understood by reference to the following non-limiting Examples:

LIST OF EXAMPLE TITLES

Example 1: Preparation of a leukocyte cDNA array comprising a candidate gene library

Example 2: Preparation of RNA from mononuclear cells for expression profiling

Example 3: Preparation of Universal Control RNA for use in leukocyte expression profiling

Example 4. RNA Labeling and hybridization to a leukocyte cDNA array of candidate nucleotide sequences.

Example 5: Clinical study for the Identification of diagnostic gene sets useful in diagnosis and treatment of Cardiac allograft rejection

Example 6: Identification of diagnostic nucleotide sets for kidney and liver allograft rejection

Example 7: Identification of diagnostic nucleotide sets for diagnosis of cytomegalovirus

Example 8: Design of oligonucleotide probes

Example 9: Production of an array of 8,000 spotted 50 mer oligonucleotides.

Example 10: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Example 11: Amplification, labeling, and hybridization of total RNA to an oligonucleotide microarray

Example 12: Real-time PCR validation of array expression results

Example 13: Real-time PCR expression markers of acute allograft rejection

Example 14: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Example 15: Correlation and Classification Analysis

Example 16: Acute allograft rejection: biopsy tissue gene expression profiling

Example 17: Microarray and PCR gene expression panels for diagnosis and monitoring of acute allograft rejection

Example 18: Assay sample preparation

Example 19: Allograft rejection diagnostic gene sequence analysis

Example 20: Detection of proteins expressed by diagnostic gene sequences

Example 21: Detecting changes in the rate of hematopoiesis

Examples

Example 1: Preparation of a leukocyte cDNA array comprising a candidate gene library

Candidate genes and gene sequences for leukocyte expression profiling are identified through methods described elsewhere in this document. Candidate genes are used to obtain or design probes for peripheral leukocyte expression profiling in a variety of ways.

A cDNA microarray carrying 384 probes was constructed using sequences selected from the initial candidate library. cDNAs is selected from T-cell libraries, PBMC libraries and buffy coat libraries.

96-Well PCR

Plasmids are isolated in 96-well format and PCR was performed in 96-well format. A master mix is made that contain the reaction buffer, dNTPs, forward and reverse primer and DNA polymerase was made. 99 ul of the master mix was aliquoted into 96-well plate. 1 ul of plasmid (1-2 ng/ul) of plasmid was added to the plate. The final reaction concentration was 10 mM Tris pH 8.3, 3.5 mM MgCl2, 25 mM KCl, 0.4 mM dNTPs, 0.4 uM M13 forward primer, 0.4 M13 reverse primer, and 10 U of Taq Gold (Applied Biosystems). The PCR conditions were:

Step 1 95C for 10 min

Step 2 95C for 15 sec

Step 3 56C for 30 sec

Step 4 72C for 2 min 15 seconds

Step 5 go to Step 2 39 times

Step 6 72C for 10 minutes

Step 7 4C for ever.

PCR Purification

PCR purification is done in a 96-well format. The ArrayIt (Telechem International, Inc.) PCR purification kit is used and the provided protocol was followed without modification. Before the

sample is evaporated to dryness, the concentration of PCR products was determined using a
spectrophotometer. After evaporation, the samples are re-suspended in 1x Micro Spotting Solution
(ArrayIt) so that the majority of the samples were between 0.2-1.0 ug/ul.

Array Fabrication

Spotted cDNA microarrays are then made from these PCR products by ArrayIt using their protocols,
which may be found at the ArrayIt website. Each fragment was spotted 3 times onto each array.
Candidate genes and gene sequences for leukocyte expression profiling are identified through methods
described elsewhere in this document. Those candidate genes are used for peripheral leukocyte
expression profiling. The candidate libraries can used to obtain or design probes for expression
profiling in a variety of ways.

Oligonucleotide probes are prepared using the gene sequences of Table 2, Table 8, and the sequence
listing. Oligo probes are designed on a contract basis by various companies (for example, Compugen,
Mergen, Affymetrix, Telechem), or designed from the candidate sequences using a variety of
parameters and algorithms as indicated at located at the MIT web site. Briefly, the length of the
oligonucleotide to be synthesized is determined, preferably greater than 18 nucleotides, generally 18-24
nucleotides, 24-70 nucleotides and, in some circumstances, more than 70 nucleotides. The sequence
analysis algorithms and tools described above are applied to the sequences to mask repetitive elements,
vector sequences and low complexity sequences. Oligonucleotides are selected that are specific to the
candidate nucleotide sequence (based on a Blast n search of the oligonucleotide sequence in question
against gene sequences databases, such as the Human Genome Sequence, UniGene, dbEST or the non-
redundant database at NCBI), and have <50% G content and 25–70% G+C content. Desired
oligonucleotides are synthesized using well-known methods and apparatus, or ordered from a company
(for example Sigma). Oligonucleotides are spotted onto microarrays. Alternatively, oligonucleotides
are synthesized directly on the array surface, using a variety of techniques (Hughes et al. 2001,
Yershov et al. 1996, Lockhart et al 1996).

Example 2: Preparation of RNA from mononuclear cells for expression profiling

Blood was isolated from the subject for leukocyte expression profiling using the following methods:
Two tubes were drawn per patient. Blood was drawn from either a standard peripheral venous blood
draw or directly from a large-bore intra-arterial or intravenous catheter inserted in the femoral artery,
femoral vein, subclavian vein or internal jugular vein. Care was taken to avoid sample contamination
with heparin from the intravascular catheters, as heparin can interfere with subsequent RNA reactions.
For each tube, 8 ml of whole blood was drawn into a tube (CPT, Becton-Dickinson order #362753)
containing the anticoagulant Citrate, 25°C density gradient solution (e.g. Ficoll, Percoll) and a
polyester gel barrier that upon centrifugation was permeable to RBCs and granulocytes but not to
mononuclear cells. The tube was inverted several times to mix the blood with the anticoagulant. The
tubes were centrifuged at 1750xg in a swing-out rotor at room temperature for 20 minutes. The tubes
were removed from the centrifuge and inverted 5-10 times to mix the plasma with the mononuclear
cells, while trapping the RBCs and the granulocytes beneath the gel barrier. The plasma/mononuclear
cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) is added. The
15ml tubes were spun for 5 minutes at 1750xg to pellet the cells. The supernatant was discarded and

1.8 ml of RLT lysis buffer is added to the mononuclear cell pellet. The buffer and cells were pipetted up and down to ensure complete lysis of the pellet. The cell lysate was frozen and stored until it is convenient to proceed with isolation of total RNA.

Total RNA was purified from the lysed mononuclear cells using the Qiagen Rneasy Miniprep kit, as directed by the manufacturer (10/99 version) for total RNA isolation, including homogenization (Qiashredder columns) and on-column DNase treatment. The purified RNA was eluted in 50ul of water. The further use of RNA prepared by this method is described in Examples 10 and 11.

Some samples were prepared by a different protocol, as follows:

Two 8 ml blood samples were drawn from a peripheral vein into a tube (CPT, Becton-Dickinson order #362753) containing anticoagulant (Citrate), 25°C density gradient solution (Ficoll) and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. The tube was inverted several times to mix the blood with the anticoagulant, and the tubes were subjected to centrifugation at 1750xg in a swing-out rotor at room temperature for 20 min. The tubes were removed from the centrifuge, and the clear plasma layer above the cloudy mononuclear cell layer was aspirated and discarded. The cloudy mononuclear cell layer was aspirated, with care taken to rinse all of the mononuclear cells from the surface of the gel barrier with PBS (phosphate buffered saline). Approximately 2 mls of mononuclear cell suspension was transferred to a 2ml microcentrifuge tube, and centrifuged for 3min. at 16,000 rpm in a microcentrifuge to pellet the cells. The supernatant was discarded and 1.8 ml of RLT lysis buffer (Qiagen) were added to the mononuclear cell pellet, which lysed the cells and inactivated Rnases. The cells and lysis buffer were pipetted up and down to ensure complete lysis of the pellet. Cell lysate was frozen and stored until it was convenient to proceed with isolation of total RNA.

RNA samples were isolated from 8 mL of whole blood. Yields ranged from 2 ug to 20ug total RNA for 8mL blood. A260/A280 spectrophotometric ratios were between 1.6 and 2.0, indicating purity of sample. 2ul of each sample were run on an agarose gel in the presence of ethidium bromide. No degradation of the RNA sample and no DNA contamination was visible.

In some cases, specific subsets of mononuclear cells were isolated from peripheral blood of human subjects. When this was done, the StemSep cell separation kits (manual version 6.0.0) were used from StemCell Technologies (Vancouver, Canada). This same protocol can be applied to the isolation of T cells, CD4 T cells, CD8 T cells, B cells, monocytes, NK cells and other cells. Isolation of cell types using negative selection with antibodies may be desirable to avoid activation of target cells by antibodies.

Example 3: Preparation of Universal Control RNA for use in leukocyte expression profiling

Control RNA was prepared using total RNA from Buffy coats and/or total RNA from enriched mononuclear cells isolated from Buffy coats, both with and without stimulation with ionomycin and PMA. The following control RNAs were prepared:

Control 1: Buffy Coat Total RNA

Control 2: Mononuclear cell Total RNA

Control 3: Stimulated buffy coat Total RNA

Control 4: Stimulated mononuclear Total RNA

Control 5: 50% Buffy coat Total RNA / 50% Stimulated buffy coat Total RNA

Control 6: 50% Mononuclear cell Total RNA / 50% Stimulated Mononuclear Total RNA

Some samples were prepared using the following protocol: Buffy coats from 38 individuals were obtained from Stanford Blood Center. Each buffy coat is derived from ~350 mL whole blood from one individual. 10 ml buffy coat was removed from the bag, and placed into a 50 ml tube. 40 ml of Buffer EL (Qiagen) was added, the tube was mixed and placed on ice for 15 minutes, then cells were pelleted by centrifugation at 2000xg for 10 minutes at 4°C. The supernatant was decanted and the cell pellet was re-suspended in 10 ml of Qiagen Buffer EL. The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The cell pellet was then re-suspended in 20 ml TRIZOL (GibcoBRL) per Buffy coat sample, the mixture was shredded using a rotary homogenizer, and the lysate was then frozen at –80°C prior to proceeding to RNA isolation.

Other control RNAs were prepared from enriched mononuclear cells prepared from Buffy coats. Buffy coats from Stanford Blood Center were obtained, as described above. 10 ml buffy coat was added to a 50 ml polypropylene tube, and 10 ml of phosphate buffer saline (PBS) was added to each tube. A polysucrose (5.7 g/dL) and sodium diatrizoate (9.0 g/dL) solution at a 1.077 +/-0.0001 g/ml density solution of equal volume to diluted sample was prepared (Histopaque 1077, Sigma cat. no 1077-1). This and all subsequent steps were performed at room temperature. 15 ml of diluted buffy coat/PBS was layered on top of 15 ml of the histopaque solution in a 50 ml tube. The tube was centrifuged at 400xg for 30 minutes at room temperature. After centrifugation, the upper layer of the solution to within 0.5 cm of the opaque interface containing the mononuclear cells was discarded. The opaque interface was transferred into a clean centrifuge tube. An equal volume of PBS was added to each tube and centrifuged at 350xg for 10 minutes at room temperature. The supernatant was discarded. 5 ml of Buffer EL (Qiagen) was used to resuspend the remaining cell pellet and the tube was centrifuged at 2000xg for 10 minutes at room temperature. The supernatant was discarded. The pellet was resuspended in 20 ml of TRIZOL (GibcoBRL) for each individual buffy coat that was processed. The sample was homogenized using a rotary homogenizer and frozen at -80C until RNA was isolated.

RNA was isolated from frozen lysed Buffy coat samples as follows: frozen samples were thawed, and 4 ml of chloroform was added to each buffy coat sample. The sample was mixed by vortexing and centrifuged at 2000xg for 5 minutes. The aqueous layer was moved to new tube and then repurified by using the RNeasy Maxi RNA clean up kit, according to the manufacturer's instruction (Qiagen, PN 75162). The yield, purity and integrity were assessed by spectrophotometer and gel electrophoresis. Some samples were prepared by a different protocol, as follows. The further use of RNA prepared using this protocol is described in Example 11.

50 whole blood samples were randomly selected from consented blood donors at the Stanford Medical School Blood Center. Each buffy coat sample was produced from ~350 mL of an individual's donated blood. The whole blood sample was centrifuged at ~4,400 x g for 8 minutes at room temperature, resulting in three distinct layers: a top layer of plasma, a second layer of buffy coat, and a third layer of red blood cells. 25 ml of the buffy coat fraction was obtained and diluted with an equal volume of PBS (phosphate buffered saline). 30 ml of diluted buffy coat was layered onto 15 ml of sodium diatrizoate

solution adjusted to a density of 1.077+/-0.001 g/ml (Histopaque 1077, Sigma) in a 50mL plastic tube. The tube was spun at 800 g for 10 minutes at room temperature. The plasma layer was removed to the 30 ml mark on the tube, and the mononuclear cell layer removed into a new tube and washed with an equal volume of PBS, and collected by centrifugation at 2000 g for 10 minutes at room temperature. The cell pellet was resuspended in 10 ml of Buffer EL (Qiagen) by vortexing and incubated on ice for 10 minutes to remove any remaining erthythrocytes. The mononuclear cells were spun at 2000 g for 10 minutes at 4 degrees Celsius. The cell pellet was lysed in 25 ml of a phenol/guanidinium thiocyanate solution (TRIZOL Reagent, Invitrogen). The sample was homogenized using a PowerGene 5 rotary homogenizer (Fisher Scientific) and Omini disposable generator probes (Fisher Scientific). The Trizol lysate was frozen at –80 degrees C until the next step.

The samples were thawed out and incubated at room temperature for 5 minutes. 5 ml chloroform was added to each sample, mixed by vortexing, and incubated at room temperature for 3 minutes. The aqueous layers were transferred to new 50 ml tubes. The aqueous layer containing total RNA was further purified using the Qiagen RNeasy Maxi kit (PN 75162), per the manufacturer's protocol (October 1999). The columns were eluted twice with 1 ml Rnase-free water, with a minute incubation before each spin. Quantity and quality of RNA was assessed using standard methods. Generally, RNA was isolated from batches of 10 buffy coats at a time, with an average yield per buffy coat of 870 µg, and an estimated total yield of 43.5 mg total RNA with a 260/280 ratio of 1.56 and a 28S/18S ratio of 1.78.

Quality of the RNA was tested using the Agilent 2100 Bioanalyzer using RNA 6000 microfluidics chips. Analysis of the electrophorgrams from the Bioanalyzer for five different batches demonstrated the reproducibility in quality between the batches.

Total RNA from all five batches were combined and mixed in a 50 ml tube, then aliquoted as follows: 2 x 10 ml aliquots in 15 ml tubes, and the rest in 100 µl aliquots in 1.5 ml microcentrifuge tubes. The aliquots gave highly reproducible results with respect to RNA purity, size and integrity. The RNA was stored at –80°C.

Test hybridization of Reference RNA.

When compared with BC38 and Stimulated mononuclear reference samples, the R50 performed as well, if not better than the other reference samples as shown in Figure 3. In an analysis of hybridizations, where the R50 targets were fluorescently labeled with Cy-5 using methods described herein and the amplified and labeled aRNA was hybridized (as in example 11) to the olignoucleotide array described in example 9. The R50 detected 97.3% of probes with a Signal to Noise ratio (S/N) of greater than three and 99.9 % of probes with S/N greater than one.

Example 4. RNA Labeling and hybridization to a leukocyte cDNA array of candidate nucleotide sequences.

Comparison of Guanine-Silica to Acid-Phenol RNA Purification (GSvsAP)

These data are from a set of 12 hybridizations designed to identify differences between the signal strength from two different RNA purification methods. The two RNA methods used were guanidine-silica (GS, Qiagen) and acid-phenol (AP, Trizol, Gibco BRL). Ten tubes of blood were drawn from each of four people. Two were used for the AP prep, the other eight were used for the GS prep. The

protocols for the leukocyte RNA preps using the AP and GS techniques were completed as described here:

Guanidine-silica (GS) method:

For each tube, 8ml blood was drawn into a tube containing the anticoagulant Citrate, 25°C density gradient solution and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. CPT tubes from Becton-Dickinson (#362753) were used for this purpose. The tube was inverted several times to mix the blood with the anticoagulant. The tubes were immediately centrifuged @1750xg in a swinging bucket rotor at room temperature for 20 min. The tubes were removed from the centrifuge and inverted 5-10 times. This mixed the plasma with the mononuclear cells, while the RBCs and the granulocytes remained trapped beneath the gel barrier. The plasma/mononuclear cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) was added. The 15ml tubes are spun for 5 minutes at 1750xg to pellet the cells. The supernatant was discarded and 1.8 ml of RLT lysis buffer (guanidine isothyocyanate) was added to the mononuclear cell pellet. The buffer and cells were pipetted up and down to ensure complete lysis of the pellet. The cell lysate was then processed exactly as described in the Qiagen Rneasy Miniprep kit protocol (10/99 version) for total RNA isolation (including steps for homogenization (Qiashredder columns) and on-column DNase treatment. The purified RNA was eluted in 50ul of water.

Acid-phenol (AP) method:

For each tube, 8ml blood was drawn into a tube containing the anticoagulant Citrate, 25°C density gradient solution and a polyester gel barrier that upon centrifugation is permeable to RBCs and granulocytes but not to mononuclear cells. The mononuclear cells and plasma remained above the barrier while the RBCs and granulocytes were trapped below. CPT tubes from Becton-Dickinson (#362753) were used for this purpose. The tube was inverted several times to mix the blood with the anticoagulant. The tubes were immediately centrifuged @1750xg in a swinging bucket rotor at room temperature for 20 min. The tubes were removed from the centrifuge and inverted 5-10 times. This mixed the plasma with the mononuclear cells, while the RBCs and the granulocytes remained trapped beneath the gel barrier. The plasma/mononuclear cell mix was decanted into a 15ml tube and 5ml of phosphate-buffered saline (PBS) was added. The 15ml tubes are spun for 5 minutes @1750xg to pellet the cells. The supernatant was discarded and the cell pellet was lysed using 0.6 mL Phenol/guanidine isothyocyanate (e.g. Trizol reagent, GibcoBRL). Subsequent total RNA isolation proceeded using the manufacturers protocol.

RNA from each person was labeled with either Cy3 or Cy5, and then hybridized in pairs to the mini-array. For instance, the first array was hybridized with GS RNA from one person (Cy3) and GS RNA from a second person (Cy5).

Techniques for labeling and hybridization for all experiments discussed here were completed as detailed above. Arrays were prepared as described in example 1.

RNA isolated from subject samples, or control Buffy coat RNA, were labeled for hybridization to a cDNA array. Total RNA (up to 100 μg) was combined with 2 μl of 100 μM solution of an Oligo

(dT)12-18 (GibcoBRL) and heated to 70°C for 10 minutes and place on ice. Reaction buffer was added to the tube, to a final concentration of 1xRT buffer (GibcoBRL), 10 mM DTT (GibcoBRL), 0.1 mM unlabeled dATP, dTTP, and dGTP, and 0.025 mM unlabeled dCTP, 200 pg of CAB (A. thaliana photosystem I chlorophyll a/b binding protein), 200 pg of RCA (A. thaliana RUBISCO activase), 0.25 mM of Cy-3 or Cy-5 dCTP, and 400 U Superscript II RT (GibcoBRL).

The volumes of each component of the labeling reaction were as follows: 20 µl of 5xRT buffer; 10 µl of 100 mM DTT; 1 µl of 10 mM dNTPs without dCTP; 0.5 µl of 5 mM CTP; 13 µl of H20; 0.02 µl of 10 ng/µl CAB and RCA; 1 µl of 40 Units/µl RNAseOUT Recombinatnt Ribonuclease Inhibitor (GibcoBRL); 2.5 µl of 1.0 mM Cy-3 or Cy-5 dCTP; and 2.0 µl of 200 Units/µl of Superscript II RT. The sample was vortexed and centrifuged. The sample was incubated at 4°C for 1 hour for first strand cDNA synthesis, then heated at 70°C for 10 minutes to quench enzymatic activity. 1 µl of 10 mg/ml of Rnase A was added to degrade the RNA strand, and the sample was incubated at 37°C for 30 minutes. Next, the Cy-3 and Cy-5 cDNA samples were combined into one tube. Unincorporated nucleotides were removed using QIAquick RCR purification protocol (Qiagen), as directed by the manufacturer. The sample was evaporated to dryness and resuspended in 5 µl of water. The sample was mixed with hybridization buffer containing 5xSSC, 0.2% SDS, 2 mg/ml Cot-1 DNA (GibcoBRL), 1 mg/ml yeast tRNA (GibcoBRL), and 1.6 ng/µl poly dA40-60 (Pharmacia). This mixture was placed on the microarray surface and a glass cover slip was placed on the array (Corning). The microarray glass slide was placed into a hybridization chamber (ArrayIt). The chamber was then submerged in a water bath overnight at 62° C. The microarray was removed from the cassette and the cover slip was removed by repeatedly submerging it to a wash buffer containing 1xSSC, and 0.1% SDS. The microarray slide was washed in 1xSSC/0.1% SDS for 5 minutes. The slide was then washed in 0.1%SSC/0.1% SDS for 5 minutes. The slide was finally washed in 0.1xSSC for 2 minutes. The slide was spun at 1000 rpm for 2 minutes to dry out the slide, then scanned on a microarray scanner (Axon Instruments, Union City, CA.).

Six hybridizations with 20 µg of RNA were performed for each type of RNA preparation (GS or AP). Since both the Cy3 and the Cy5 labeled RNA are from test preparations, there are six data points for each GS prepped, Cy3-labeled RNA and six for each GS-prepped, Cy5-labeled RNA. The mini array hybridizations were scanned on and Axon Instruments scanner using GenPix 3.0 software. The data presented were derived as follows. First, all features flagged as "not found" by the software were removed from the dataset for individual hybridizations. These features are usually due to high local background or other processing artifacts. Second, the median fluorescence intensity minus the background fluorescence intensity was used to calculate the mean background subtracted signal for each dye for each hybridization. In Figure 3, the mean of these means across all six hybridizations is graphed (n=6 for each column). The error bars are the SEM. This experiment shows that the average signal from AP prepared RNA is 47% of the average signal from GS prepared RNA for both Cy3 and Cy5.

Generation of expression data for leukocyte genes from peripheral leukocyte samples

Six hybridizations were performed with RNA purified from human blood leukocytes using the protocols given above. Four of the six were prepared using the GS method and 2 were prepared using

the AP method. Each preparation of leukocyte RNA was labeled with Cy3 and 10 μg hybridized to the mini-array. A control RNA was batch labeled with Cy5 and 10 μg hybridized to each mini-array together with the Cy3-labeled experimental RNA.

The control RNA used for these experiments was Control 1: Buffy Coat RNA, as described above. The protocol for the preparation of that RNA is reproduced here:

<u>Buffy Coat RNA Isolation:</u>

Buffy coats were obtained from Stanford Blood Center (in total 38 individual buffy coats were used. Each buffy coat is derived from ~350 mL whole blood from one individual. 10 ml buffy coat was taken and placed into a 50 ml tube and 40 ml of a hypoclorous acid (HOCl) solution (Buffer EL from Qiagen) was added. The tube was mixed and placed on ice for 15 minutes. The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The supernatant was decanted and the cell pellet was re-suspended in 10 ml of hypochlorous acid solution (Qiagen Buffer EL). The tube was then centrifuged at 2000xg for 10 minutes at 4°C. The cell pellet was then re-suspended in 20 ml phenol/guanidine thiocyanate solution (TRIZOL from GibcoBRL) for each individual buffy coat that was processed. The mixture was then shredded using a rotary homogenizer. The lysate was then frozen at –80°C prior to proceeding to RNA isolation.

The arrays were then scanned and analyzed on an Axon Instruments scanner using GenePix 3.0 software. The data presented were derived as follows. First, all features flagged as "not found" by the software were removed from the dataset for individual hybridizations. Second, control features were used to normalize the data for labeling and hybridization variability within the experiment. The control features are cDNA for genes from the plant, *Arabidopsis thaliana*, that were included when spotting the mini-array. Equal amounts of RNA complementary to two of these cDNAs were added to each of the samples before they were labeled. A third was pre-labeled and equal amounts were added to each hybridization solution before hybridization. Using the signal from these genes, we derived a normalization constant (L_j) according to the following formula:

$$L_j = \frac{\dfrac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{\dfrac{\sum_{j=1}^{K} \dfrac{\sum_{i=1}^{N} BGSS_{j,i}}{N}}{K}}$$

where $BGSS_i$ is the signal for a specific feature as identified in the GenePix software as the median background subtracted signal for that feature, N is the number of $A.$ *thaliana* control features, K is the number of hybridizations, and L is the normalization constant for each individual hybridization. Using the formula above, the mean over all control features of a particular hybridization and dye (eg Cy3) was calculated. Then these control feature means for all Cy3 hybridizations were averaged. The

control feature mean in one hybridization divided by the average of all hybridizations gives a
normalization constant for that particular Cy3 hybridization.

The same normalization steps were performed for Cy3 and Cy5 values, both fluorescence and
background. Once normalized, the background Cy3 fluorescence was subtracted from the Cy3
fluorescence for each feature. Values less than 100 were eliminated from further calculations since low
values caused spurious results.

Figure 4 shows the average background subtracted signal for each of nine leukocyte-specific genes on
the mini array. This average is for 3-6 of the above-described hybridizations for each gene. The error
bars are the SEM.

The ratio of Cy3 to Cy5 signal is shown for a number of genes. This ratio corrects for variability
among hybridizations and allows comparison between experiments done at different times. The ratio is
calculated as the Cy3 background subtracted signal divided by the Cy5 background subtracted signal.
Each bar is the average for 3-6 hybridizations. The error bars are SEM.

Together, these results show that we can measure expression levels for genes that are expressed
specifically in sub-populations of leukocytes. These expression measurements were made with only 10
μg of leukocyte total RNA that was labeled directly by reverse transcription. The signal strength can
be increased by improved labeling techniques that amplify either the starting RNA or the signal
fluorescence. In addition, scanning techniques with higher sensitivity can be used.

Genes in Figures 4 and 5:

Gene Name/Description	GenBank Accession Number	Gene Name Abbreviation
T cell-specific tyrosine kinase Mrna	L10717	TKTCS
Interleukin 1 alpha (IL 1) mRNA, complete cds	NM_000575	IL1A
T-cell surface antigen CD2 (T11) mRNA, complete cds	M14362	CD2
Interleukin-13 (IL-13) precursor gene, complete cds	U31120	IL-13
Thymocyte antigen CD1a mRNA, complete cds	M28825	CD1a
CD6 mRNA for T cell glycoprotein CDS	NM_006725	CD6
MHC class II HLA-DQA1 mRNA, complete cds	U77589	HLA-DQA1
Granulocyte colony-stimulating factor	M28170	CD19
Homo sapiens CD69 antigen	NM_001781	CD69

*Example 5: Clinical study to identify diagnostic gene sets useful in diagnosis and treatment of cardiac
allograft recipients*

An observational study was conducted in which a prospective cohort of cardiac transplant recipients
were analyzed for associations between clinical events or rejection grades and expression of a
leukocyte candidate nucleotide sequence library. Patients were identified at 4 cardiac transplantation

centers while on the transplant waiting list or during their routing post-transplant care. All adult cardiac transplant recipients (new or re-transplants) who received an organ at the study center during the study period or within 3 months of the start of the study period were eligible. The first year after transplantation is the time when most acute rejection occurs and it is thus important to study patients during this period. Patients provided informed consent prior to study procedures.

Peripheral blood leukocyte samples were obtained from all patients at the following time points: prior to transplant surgery (when able), the same day as routinely scheduled screening biopsies, upon evaluation for suspected acute rejection (urgent biopsies), on hospitalization for an acute complication of transplantation or immunosuppression, and when Cytomegalovirus (CMV) infection was suspected or confirmed. Samples were obtained through a standard peripheral vein blood draw or through a catheter placed for patient care (for example, a central venous catheter placed for endocardial biopsy). When blood was drawn from a intravenous line, care was taken to avoid obtaining heparin with the sample as it can interfere with downstream reactions involving the RNA. Mononuclear cells were prepared from whole blood samples as described in Example 2. Samples were processed within 2 hours of the blood draw and DNA and serum were saved in addition to RNA. Samples were stored at −80° C or on dry ice and sent to the site of RNA preparation in a sealed container with ample dry ice. RNA was isolated from subject samples as described in Example 2 and hybridized to a candidate library of differentially expressed leukocyte nucleotide sequences, as further described in Examples 9-10. Methods used for amplification, labeling, hybridization and scanning are described in Example 11. Analysis of human transplant patient mononuclear cell RNA hybridized to a microarray and identification of diagnostic gene sets is shown in Example 10.

From each patient, clinical information was obtained at the following time points: prior to transplant surgery (when available), the same day as routinely scheduled screening biopsies, upon evaluation for suspected acute rejection (e.g., urgent biopsies), on hospitalization for an acute complication of transplantation or immunosuppression, and when Cytomegalovirus (CMV) infection was suspected or confirmed. Data was collected directly from the patient, from the patient's medical record, from diagnostic test reports or from computerized hospital databases. It was important to collect all information pertaining to the study clinical correlates (diagnoses and patient events and states to which expression data is correlated) and confounding variables (diagnoses and patient events and states that may result in altered leukocyte gene expression. Examples of clinical data collected are: patient sex, date of birth, date of transplant, race, requirement for prospective cross match, occurrence of pre-transplant diagnoses and complications, indication for transplantation, severity and type of heart disease, history of left ventricular assist devices, all known medical diagnoses, blood type, HLA type, viral serologies (including CMV, Hepatitis B and C, HIV and others), serum chemistries, white and red blood cell counts and differentials, CMV infections (clinical manifestations and methods of diagnosis), occurrence of new cancer, hemodynamic parameters measured by catheterization of the right or left heart (measures of graft function), results of echocardiography, results of coronary angiograms, results of intravascular ultrasound studies (diagnosis of transplant vasculopathy), medications, changes in medications, treatments for rejection, and medication levels. Information was also collected regarding the organ donor, including demographics, blood type, HLA type, results of screening cultures, results

of viral serologies, primary cause of brain death, the need for inotropic support, and the organ cold ischemia time.

Of great importance was the collection of the results of endocardial biopsy for each of the patients at each visit. Biopsy results were all interpreted and recorded using the international society for heart and lung transplantation (ISHLT) criteria, described below. Biopsy pathological grades were determined by experienced pathologists at each center.

ISHLT Criteria

Grade	Finding	Rejection Severity
0	No lymphocytic infiltrates	None
1A	Focal (perivascular or interstitial lymphocytic infiltrates without necrosis)	Borderline mild
1B	Diffuse but sparse lymphocytic infiltrates without necrosis	Mild
2	One focus only with aggressive lymphocytic infiltrate and/or myocyte damage	Mild, focal moderate
3A	Multifocal aggressive lymphocytic infiltrates and/or myocardial damage	Moderate
3B	Diffuse inflammatory lymphocytic infiltrates with necrosis	Borderline Severe
4	Diffuse aggressive polymorphous lymphocytic infiltrates with edema hemorrhage and vasculitis, with necrosis	Severe

Because variability exists in the assignment of ISHLT grades, it was important to have a centralized and blinded reading of the biopsy slides by a single pathologist. This was arranged for all biopsy slides associated with samples in the analysis. Slides were obtained and assigned an encoded number. A single pathologist then read all slides from all centers and assigned an ISHLT grade. Grades from the single pathologist were then compared to the original grades derived from the pathologists at the study centers. For the purposes of correlation analysis of leukocyte gene expression to biopsy grades, the centralized reading information was used in a variety of ways (see Example 10 for more detail). In some analyses, only the original reading was used as an outcome. In other analyses, the result from the centralized reader was used as an outcome. In other analyses, the highest of the 2 grades was used. For example, if the original assigned grade was 0 and the centralized reader assigned a 1A, then 1A was the grade used as an outcome. In some analyses, the highest grade was used and then samples associated with a Grade 1A reading were excluded from the analysis. In some analyses, only grades with no disagreement between the 2 readings were used as outcomes for correlation analysis.

Clinical data was entered and stored in a database. The database was queried to identify all patients and patient visits that meet desired criteria (for example, patients with > grade II biopsy results, no CMV infection and time since transplant < 12 weeks).

The collected clinical data (disease criteria) is used to define patient or sample groups for correlation of expression data. Patient groups are identified for comparison, for example, a patient group that possesses a useful or interesting clinical distinction, versus a patient group that does not possess the distinction. Examples of useful and interesting patient distinctions that can be made on the basis of collected clinical data are listed here:

1.   Rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteroids, anti-T cell antibodies, or total lymphoid irradiation.

2.   Rejection with histologic grade 2 or higher.

3.   Rejection with histologic grade <2.

4.   The absence of histologic rejection <u>and</u> normal or unchanged allograft function (based on hemodynamic measurements from catheterization or on echocardiographic data).

5.   The presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on hemodynamic measurements from catheterization or on echocardiographic data).

6.   Documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection.

7.   Specific graft biopsy rejection grades

8.   Rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen

9.   Rejection of mild to moderate severity with allograft dysfunction prompting plasmaphoresis or a diagnosis of "humoral" rejection

10.   Infections other than CMV, esp. Epstein Barr virus (EBV)

11.   Lymphoproliferative disorder (also called, post-transplant lymphoma)

12.   Transplant vasculopathy diagnosed by increased intimal thickness on intravascular ultrasound (IVUS), angiography, or acute myocardial infarction.

13.   Graft Failure or Retransplantation

14. All cause mortality

15.   Grade 1A or higher rejection as defined by the initial biopsy reading.

16. Grade 1B or higher rejection as defined by the initial biopsy reading.

17.   Grade 1A or higher rejection as defined by the centralized biopsy reading.

18. Grade 1B or higher rejection as defined by the centralized biopsy reading.

19.   Grade 1A or higher rejection as defined by the highest of the initial and centralized biopsy reading.

20.   Grade 1B or higher rejection as defined by the highest of the initial and centralized biopsy reading.

21. Any rejection > Grade 2 occurring in patient at any time in the post-transplant course.

Expression profiles of subject samples are examined to discover sets of nucleotide sequences with differential expression between patient groups, for example, by methods describes above and below. Non-limiting examples of patient leukocyte samples to obtain for discovery of various diagnostic nucleotide sets are as follows:

Leukocyte set to avoid biopsy or select for biopsy:
Samples : Grade 0 vs. Grades 1-4

Leukocyte set to monitor therapeutic response:
Examine successful vs. unsuccessful drug treatment.

Samples:
Successful: Time 1: rejection, Time 2: drug therapy Time 3: no rejection
    Unsuccessful: Time 1: rejection, Time 2: drug-therapy; Time 3: rejection · ·

Leukocyte set to predict subsequent acute rejection. '
Biopsy may show no rejection, but the patient may develop rejection shortly thereafter. Look at
profiles of patients who subsequently do and do not develop rejection.

Samples:
Group 1 (Subsequent rejection): Time 1: Grade 0; Time 2: Grade>0
Group 2 (No subsequent rejection): Time 1: Grade 0; Time 2: Grade 0

Focal rejection may be missed by biopsy. When this occurs the patient may have a Grade 0, but
actually has rejection. These patients may go on to have damage to the graft etc.

Samples:
Non-rejectors: no rejection over some period of time
Rejectors: an episode of rejection over same period

Leukocyte set to diagnose subsequent or current graft failure:

Samples:
Echocardiographic or catheterization data to define worsening function over time and correlate to
profiles.

Leukocyte set to diagnose impending active CMV:

Samples:
Look at patients who are CMV IgG positive. Compare patients with subsequent (to a sample) clinical
CMV infection verses no subsequent clinical CMV infection.

Leukocyte set to diagnose current active CMV:

Samples:
Analyze patients who are CMV IgG positive. Compare patients with active current clinical CMV
infection vs. no active current CMV infection.

Upon identification of a nucleotide sequence or set of nucleotide sequences that distinguish patient

groups with a high degree of accuracy, that nucleotide sequence or set of nucleotide sequences is

· validated, and implemented as a diagnostic test. The use of the test depends on the patient groups that

are used to discover the nucleotide set. For example, if a set of nucleotide sequences is discovered that

have collective expression behavior that reliably distinguishes patients with no histological rejection or

graft dysfunction from all others, a diagnostic is developed that is used to screen patients for the need

for biopsy. Patients identified as having no rejection do not need biopsy, while others are subjected to

a biopsy to further define the extent of disease. In another example, a diagnostic nucleotide set that

determines continuing graft rejection associated with myocyte necrosis (> grade I) is used to determine

that a patient is not receiving adequate treatment under the current treatment regimen. After increased

or altered immunosuppressive therapy, diagnostic profiling is conducted to determine whether continuing graft rejection is progressing. In yet another example, a diagnostic nucleotide set(s) that determine a patient's rejection status and diagnose cytomegalovirus infection is used to balance immunosuppressive and anti-viral therapy.

The methods of this example are also applicable to cardiac xenograft monitoring.

Example 6: Identification of diagnostic nucleotide sets for kidney and liver allograft rejection

Diagnostic tests for rejection are identified using patient leukocyte expression profiles to identify a molecular signature correlated with rejection of a transplanted kidney or liver. Blood, or other leukocyte source, samples are obtained from patients undergoing kidney or liver biopsy following liver or kidney transplantation, respectively. Such results reveal the histological grade, i.e., the state and severity of allograft rejection. Expression profiles are obtained from the samples as described above, and the expression profile is correlated with biopsy results. In the case of kidney rejection, clinical data is collected corresponding to urine output, level of creatine clearance, and level of serum creatine (and other markers of renal function). Clinical data collected for monitoring liver transplant rejection includes, biochemical characterization of serum markers of liver damage and function such as SGOT, SGPT, Alkaline phosphatase, GGT, Bilirubin, Albumin and Prothrombin time.

Leukocyte nucleotide sequence expression profiles are collected and correlated with important clinical states and outcomes in renal or hepatic transplantation. Examples of useful clinical correlates are given here:

1.   Rejection episode of at least moderate histologic grade, which results in treatment of the patient with additional corticosteriods, anti-T cell antibodies, or total lymphoid irradiation.

2.   The absence of histologic rejection and normal or unchanged allograft function (based on tests of renal or liver function listed above).

3.   The presence of severe allograft dysfunction or worsening allograft dysfunction during the study period (based on tests of renal and hepatic function listed above).

4.   Documented CMV infection by culture, histology, or PCR, and at least one clinical sign or symptom of infection.

5.   Specific graft biopsy rejection grades

6.   Rejection of mild to moderate histologic severity prompting augmentation of the patient's chronic immunosuppressive regimen

7.   Infections other than CMV, esp. Epstein Barr virus (EBV)

8.   Lymphoproliferative disorder (also called, post-transplant lymphoma)

9.   Graft Failure or Retransplantation

10.   Need for hemodialysis or other renal replacement therapy for renal transplant patients.

11.   Hepatic encephalopathy for liver transplant recipients.

12.   All cause mortality

Subsets of the candidate library (or of a previously identified diagnostic nucleotide set), are identified, according to the above procedures, that have predictive and/or diagnostic value for kidney or liver allograft rejection.

Example 7: Identification of a diagnostic nucleotide set for diagnosis of cytomegalovirus

Cytomegalovirus is a very important cause of disease in immunocompromised patients, for example, transplant patients, cancer patients, and AIDS patients. The virus can cause inflammation and disease in almost any tissue (particularly the colon, lung, bone marrow and retina). It is increasingly important to identify patients with current or impending clinical CMV disease, particularly when immunosuppressive drugs are to be used in a patient, e.g. for preventing transplant rejection.

Leukocytes are profiled in patients with active CMV, impending CMV, or no CMV. Expression profiles correlating with diagnosis of active or impending CMV are identified. Subsets of the candidate library (or a previously identified diagnostic nucleotide set) are identified, according to the above procedures that have predictive value for the diagnosis of active or impending CMV. Diagnostic nucleotide set(s) identified with predictive value for the diagnosis of active or impending CMV may be combined, or used in conjunction with, cardiac, liver and/or kidney allograft-related diagnostic gene set(s) (described in Examples 6 and 10).

In addition, or alternatively, CMV nucleotide sequences are obtained, and a diagnostic nucleotide set is designed using CMV nucleotide sequence. The entire sequence of the organism is known and all CMV nucleotide sequences can be isolated and added to the library using the sequence information and the approach described below. Known expressed genes are preferred. Alternatively, nucleotide sequences are selected to represent groups of CMV genes that are coordinately expressed (immediate early genes, early genes, and late genes) (Spector et al. 1990, Stamminger et al. 1990).

Oligonucleotides were designed for CMV genes using the oligo design procedures of Example 8. Probes were designed using the 14 gene sequences shown here and were included on the array described in example 9:

	HCMVTRL2 (IRL2)	1893..2240
	HCMVTRL7 (IRL7)	complement(6595..6843)
	HCMVUL21	complement(26497..27024)
	HCMVUL27	complement(32831..34657)
	HCMVUL33	43251..44423
Cytomegalovirus (CMV) Accession #X17403	HCMVUL54	complement(76903..80631)
	HCMVUL75	complement(107901..110132)
	HCMVUL83	complement(119352..121037)
	HCMVUL106	complement(154947..155324)
	HCMVUL109	complement(157514..157810)
	HCMVUL113	161503..162800
	HCMVUL122	complement(169364..170599)
	HCMVUL123 (last exon at 3'-end)	complement(171006..172225)
	HCMVUS28	219200..220171

Diagnostic nucleotide set(s) for expression of CMV genes is used in combination with diagnostic leukocyte nucleotide sets for diagnosis of other conditions, e.g. organ allograft rejection.

Using the techniques described in example 2 mononuclear samples from 180 cardiac transplant recipients (enrolled in the study described in Example 5) were used for expression profiling with the leukocyte arrays. Of these samples 15 were associated with patients who had a diagnosis of primary or reactivation CMV made by culture, PCR or any specific diagnostic test.

After preparation of RNA, amplification, labeling, hybridization, scanning, feature extraction and data processing were done as described in Example 11 using the oligonucleotide microarrays described in Example 9.

The resulting log ratio of expression of Cy3 (patient sample)/ Cy5 (R50 reference RNA) was used for analysis. Significance analysis for microarrays (SAM, Tusher 2001, see Example 15) was applied to determine which genes were most significantly differentially expressed between these 15 CMV patients and the 165 non-CMV patients (Table 12). 12 genes were identified with a 0% FDR and 6 with a 0.1% FDR and are listed in Table 2. Some genes are represented by more than one oligonucleotide on the array and for 2 genes, multiple oligonucleotides from the same gene are called significant (SEQ IDs: 3061, 3064: eomesodermin and 3031, 3040, 104, 2736: small inducible cytokine A4).

Clinical variables were also included in the significance analysis. For example, the white blood cell count and the number of weeks post transplant (for the patient at the time the sample was obtained) were available for most of the 180 samples. The log of these variables was taken and the variables were then used in the significance analysis described above with the gene expression data. Both the white blood cell count (0.1% FDR) and the weeks post transplant (0% FDR) appeared to correlate with CMV status. CMV patients were more likely to have samples associated with later post transplant data and the lower white blood cell counts.

These genes and variables can be used alone or in association with other genes or variables or with other genes to build a diagnostic gene set or a classification algorithm using the approaches described herein.

Primers for real-time PCR validation were designed for some of these genes as described in Example 13 and listed in Table 2C and the sequence listing. Using the methods described in example 13, primers for Granzyme B were designed and used to validate expression findings from the arrays. 6 samples were tested (3 from patients with CMV and 3 from patients without CMV). The gene was found to be differentially expressed between the patients with and without CMV (see example 13 for full description). This same approach can be used to validate other diagnostic genes by real-time PCR. Diagnostic nucleotide sets can also be identified for a variety of other viral diseases (Table 1) using this same approach.

cDNA microarrays may be used to monitor viral expression. In addition, these methods may be used to monitor other viruses, such as Epstein-Barr virus, Herpes Simplex 1 and vesicular stomatitis virus.

Example 8- Design of oligonucleotide probes

By way of example, this section describes the design of four oligonucleotide probes using Array Designer Ver 1.1 (Premier Biosoft International, Palo Alto, CA). The major steps in the process are given first.

Obtain best possible sequence of mRNA from GenBank. If a full-length sequence reference sequence is not available, a partial sequence is used, with preference for the 3' end over the 5' end. When the

sequence is known to represent the antisense strand, the reverse complement of the sequence is used for

probe design. For sequences represented in the subtracted leukocyte expression library that have no

significant match in GenBank at the time of probe design, our sequence is used.

Mask low complexity regions and repetitive elements in the sequence using an algorithm such as

RepeatMasker.

Use probe design software, such as Array Designer, version 1.1, to select a sequence of 50 residues

with specified physical and chemical properties. The 50 residues nearest the 3' end constitute a search

frame. The residues it contains are tested for suitability. If they don't meet the specified criteria, the

search frame is moved one residue closer to the 5' end, and the 50 residues it now contains are tested.

The process is repeated until a suitable 50-mer is found.

If no such 50-mer occurs in the sequence, the physical and chemical criteria are adjusted until a suitable

50-mer is found.

Compare the probe to dbEST, the UniGene cluster set, and the assembled human genome using the

BLASTn search tool at NCBI to obtain the pertinent identifying information and to verify that the

probe does not have significant similarity to more than one known gene.

<u>Clone 40H12</u>

Clone 40H12 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using

the BLAST search tool. The sequence matched accession number NM_002310, a 'curated RefSeq

project' sequence, see Pruitt et al. (2000) <u>Trends Genet.</u> 16:44-47, encoding leukemia inhibitory factor

receptor (LIFR) mRNA with a reported E value of zero. An E value of zero indicates there is, for all

practical purposes, no chance that the similarity was random based on the length of the sequence and .

the composition and size of the database. This sequence, cataloged by accession number NM_002310,

is much longer than the sequence of clone 40H12 and has a poly-A tail. This indicated that the

sequence cataloged by accession number NM_002310 is the sense strand and a more complete

representation of the mRNA than the sequence of clone 40H12, especially at the 3' end. Accession

number "NM_002310" was included in a text file of accession numbers representing sense strand

mRNAs, and sequences for the sense strand mRNAs were obtained by uploading a text file containing

desired accession numbers as an Entrez search query using the Batch Entrez web interface and saving

the results locally as a FASTA file. The following sequence was obtained, and the region of alignment

of clone 40H12 is outlined:

```
CTCTCTCCCAGAACGTGTCTCTGCTGCAAGGCACCGGGCCCTTTCGCTCTGCAGAACTGCACTTGCAAGA
CCATTATCAACTCCTAATCCCAGCTCAGAAAGGGAGCCTCTGCGACTCATTCATCGCCCTCCAGGACTGA
CTGCATTGCACAGATGATGGATATTTACGTATGTTTGAAACGACCATCCTGGATGGTGGACAATAAAAGA
ATGAGGACTGCTTCAAATTTCCAGTGGCTGTTATCAACATTTATTCTTCTATATCTAATGAATCAAGTAA
ATAGCCAGAAAAAGGGGGCTCCTCATGATTTGAAGTGTGTAACTAACAATTTGCAAGTGTGGAACTGTTC
TTGGAAAGCACCCTCTGGAACAGGCCGTGGTACTGATTATGAAGTTTGCATTGAAAACAGGTCCCGTTCT
TGTTATCAGTTGGAGAAAACCAGTATTAAAATTCCAGCTCTTTCACATGGTGATTATGAAATAACAATAA
ATTCTCTACATGATTTTGGAAGTTCTACAAGTAAATTCACACTAAATGAACAAAACGTTTCCTTAATTCC
AGATACTCCAGAGATCTTGAATTTGTCTGCTGATTTCTCAACCTCTACATTATACCTAAAGTGGAACGAC
AGGGGTTCAGTTTTTCCACACCGCTCAAATGTTATCTGGGAAATTAAAGTTCTACGTAAAGAGAGTATGG
AGCTCGTAAAATTAGTGACCCACAACACAACTCTGAATGGCAAAGATACACTTCATCACTGGAGTTGGGC
CTCAGATATGCCCTTGGAATGTGCCATTCATTTTGTGGAAATTAGATGCTACATTGACAATCTTCATTTT
TCTGGTCTCGAAGAGTGGAGTGACTGGAGCCCTGTGAAGAACATTTCTTGGATACCTGATTCTCAGACTA
AGGTTTTTCCTCAAGATAAAGTGATACTTGTAGGCTCAGACATAACATTTTGTTGTGTGAGTCAAGAAAA
```

AGTGTTATCAGCACTGATTGGCCATACAAACTGCCCCTTGATCCATCTTGATGGGGAAAATGTTGCAATC
AAGATTCGTAATATTTCTGTTTCTGCAAGTAGTGGAACAAATGTAGTTTTTACAACCGAAGATAACATAT
TTGGAACCGTTATTTTTGCTGGATATCCACCAGATACTCCTCAACAACTGAATTGTGAGACACATGATTT
AAAAGAAATTATATGTAGTTGGAATCCAGGAAGGGTGACAGCGTTGGTGGGCCCACGTGCTACAAGCTAC
ACTTTAGTTGAAAGTTTTTCAGGAAAATATGTTAGACTTAAAAGAGCTGAAGCACCTACAAACGAAAGCT
ATCAATTATTATTTCAAATGCTTCCAAATCAAGAAATATATAATTTTACTTTGAATGCTCACAATCCGCT
GGGTCGATCACAATCAACAATTTTAGTTAATATAACTGAAAAAGTTTATCCCCATACTCCTACTTCATTC
AAAGTGAAGGATATTAATTCAACAGCTGTTAAACTTTCTTGGCATTTACCAGGCAACTTTGCAAAGATTA
ATTTTTTATGTGAAATTGAAATTAAGAAATCTAATTCAGTACAAGAGCAGCGGAATGTCACAATCAAAGG
AGTAGAAAATTCAAGTTATCTTGTTGCTCTGGACAAGTTAAATCCATACACTCTATATACTTTTCGGATT
CGTTGTTCTACTGAAACTTTCTGGAAATGGAGCAAATGGAGCAATAAAAAACAACATTTAACAACAGAAG
CCAGTCCTTCAAAGGGGCCTGATACTTGGAGAGAGTGGAGTTCTGATGGAAAAAATTTAATAATCTATTG
GAAGCCTTTACCCATTAATGAAGCTAATGGAAAAATACTTTCCTACAATGTATCGTGTTCATCAGATGAG
GAAACACAGTCCCTTTCTGAAATCCCTGATCCTCAGCACAAAGCAGAGATACGACTTGATAAGAATGACT
ACATCATCAGCGTAGTGGCTAAAAATTCTGTGGGCTCATCACCACCTTCCAAAATAGCGAGTATGGAAAT
TCCAAATGATGATCTCAAAATAGAACAAGTTGTTGGGATGGGAAAGGGGATTCTCCTCACCTGGCATTAC
GACCCCAACATGACTTGCGACTACGTCATTAAGTGGTGTAACTCGTCTCGGTCGGAACCATGCCTTATGG
ACTGGAGAAAGTTCCCTCAAACAGCACTGAAACTGTAATAGAATCTGATGAGTTTCGACCAGGTATAAG
ATATAATTTTTTCCTGTATGGATGCAGAAATCAAGGATATCAATTATTACGCTCCATGATTGGATATATA
GAAGAATTGGCTCCCATTGTTGCACCAAATTTTACTGTTGAGGATACTTCTGCAGATTCGATATTAGTAA
AATGGGAAGACATTCCTGTGGAAGAACTTAGAGGCTTTTTAAGAGGATATTTGTTTTACTTTGGAAAAGG
AGAAAGAGACACATCTAAGATGAGGGTTTTAGAATCAGGTCGTTCTGACATAAAAGTTAAGAATATTACT
GACATATCCCAGAAGACACTGAGAATTGCTGATCTTCAAGGTAAAACAAGTTACCACCTGGTCTTGCGAG
CCTATACAGATGGTGGAGTGGGCCCGGAGAAGAGTATGTATGTGGTGACAAAGGAAAATTCTGTGGGATT
AATTATTGCCATTCTCATCCCAGTGGCAGTGGCTGTCATTGTTGGAGTGGTGACAAGTATCCTTTGCTAT
CGGAAACGAGAATGGATTAAAGAAACCTTCTACCTGATATTCCAAATCCAGAAAACTGTAAAGCATTAC
AGTTTCAAAAGAGTGTCTGTGAGGGAAGCAGTGCTCTTAAAACATTGGAAATGAATCCTTGTACCCCAAA
TAATGTTGAGGTTCTGGAAACTCGATCAGCATTTCCTAAAATAGAAGATACAGAAATAATTTCCCCAGTA
GCTGAGCGTCCTGAAGATCGCTCTGATGCAGAGCCTGAAAACCATGTGGTTGTGTCCTATTGTCCACCCA
TCATTGAGGAAGAAATACCAAACCCAGCCGCAGATGAAGCTGGAGGGACTGCACAGGTTATTTACATTGA
TGTTCAGTCGATGTATCAGCCTCAAGCAAAACCAGAAGAAGAACAAGAAATGACCCTGTAGGAGGGGCA
GGCTATAAGCCACAGATGCACCTCCCCATTAATTCTACTGTGGAAGATATAGCTGCAGAAGAGGACTTAG
ATAAAACTGCGGGTTACAGACCTCAGGCCAATGTAAATACATGGAATTTAGTGTCTCCAGACTCTCCTAG
ATCCATAGACAGCAACAGTGAGATTGTCTCATTTGGAAGTCCATGCTCCATTAATTCCCGACAATTTTTG
ATTCCTCCTAAAGATGAAGACTCTCCTAAATCTAATGGAGGAGGGTGGTCCTTTACAAACTTTTTTCAGA
ACAAACCAAACGATTAACAGTGTCACCGTGTCACTTCAGTCAGCCATCTCAATAAGCTCTTACTGCTAGT
GTTGCTACATCAGCACTGGGCATTCTTGGAGGGATCCTGTGAAGTATTGTTAGGAGGTGAACTTCACTAC
ATGTTAAGTTACACTGAAAGTTCATGTGCTTTTAATGTAGTCTAAAAGCCAAAGTATAGTGACTCAGAAT
CCTCAATCCACAAAACTCAAGATTGGGAGCTCTTTGTGATCAAGCCAAAGAATTCTCATGTACTCTACCT
TCAAGAAGCATTTCAAGGCTAATACCTACTTGTACGTACATGTAAAACAAATCCCGCCGCAACTGTTTTC
TGTTCTGTTGTTTGTGGTTTTCTCATATGTATACTTGGTGGAATTGTAAGTGGATTTGCAGGCCAGGGAG
AAAATGTCCAAGTAACAGGTGAAGTTTATTTGCCTGACGTTTACTCCTTTCTAGATGAAAACCAAGCACA
GATTTTAAAACTTCTAAGATTATTCTCCTCTATCCACAGCATTCACAAAAATTAATATAATTTTTAATGT
AGTGACAGCGATTTAGTGTTTTGTTTGATAAAGTATGCTTATTTCTGTGCCTACTGTATAATGGTTATCA
AACAGTTGTCTCAGGGGTACAAACTTTGAAAACAAGTGTGACACTGACCAGCCCAAAT┌CATAATCATGTT┐
└TTCTTGCTGTGATAGGTTTTGCTTGCCTTTTCATTATTTTTTAGCTTTTATGCTTGCTTCCATTATTTCA┐
└GTTGGTTGCCCTAATATTTAAAATTTACACTTCTAAGACTAGAGACCCACATTTTTTAAAAATCATTTTA┐
└TTTTGTGATACAGTGACAGCTTTATATGAGCAAATTCAATATTATTCATAAGCATGTAATTCCAGTGACT┐
└TACTATGTGAGATGACTACTAAGCAATATCTAGCAGCGTTAGTTCCATATAGTTCTGATTGGATTTCGTT┐
└CCTCCTGAGGAGACCATGCCGTTGAGCTTGGCTACCCAGGCAGTGGTGATCTTTGACACCTTCTGGTGGA┐
└TGTTCCTCCCACTCATGAGTCTTTTCATCATGCCACATTATCTGATCCAGTCCTCACATTTTTAAATATA┐
└AAACTAAAGAGAGAATGCTTCTTACAGGAACAGTTACCCAAGGGCTGTTTCTTAGTAACTGTCATAAACT┐
└GATCTGGATCCATGGGCATACCTGTGTTCGAGGTGCAGCAATTGCTTGGTGAGCTGTGCAGAATTGATTG┐
└CCTTCAGCACAGCATCCTCTGCCCACCCTTGTTTCTCATAAGCGATGTCTGGAGTGATTGTGGTTCTTGG┐
└AAAAGCAGAAGGAAAAACTAAAAAGTGTATCTTGTATTTTCCCTGCC┘CTCAGGTTGCCTATGTATTTTAC
CTTTTCATATTTAAGGCAAAAGTACTTGAAAATTTTAAGTGTCCGAATAAGATATGTCTTTTTTGTTTGT
TTTTTTTGGTTGGTTGTTTGTTTTTTATCATCTGAGATTCTGTAATGTATTTGCAAATAATGGATCAATT
AATTTTTTTTGAAGCTCATATTGTATCTTTTTAAAAACCATGTTGTGGAAAAAAGCCAGAGTGACAAGTG
ACAAAATCTATTTAGGAACTCTGTGTATGAATCCTGATTTTAACTGCTAGGATTCAGCTAAATTTCTGAG
CTTTATGATCTGTGGAAATTTGGAATGAAATCGAATTCATTTTGTACATACATAGTATATTAAAACTATA

TAATAGTTCATAGAAATGTTCAGTAATGAAAAAATATATCCAATCAGAGCCATCCCGAAAAAAAAAAAA
AA (SEQ ID NO: 3101)

The FASTA file, including the sequence of NM_002310, was masked using the RepeatMasker web

interface (Smit, AFA & Green, P RepeatMasker at

http://ftp.genome.washington.edu/RM/RepeatMasker.html, Smit and Green). Specifically, during

masking, the following types of sequences were replaced with "N's": SINE/MIR & LINE/L2, LINE/L1

, LTR/MaLR, LTR/Retroviral , Alu, and other low informational content sequences such as simple

repeats. Below is the sequence following masking:

CTCTCTCCCAGAACGTGTCTCTGCTGCAAGGCACCGGGCCCTTTCGCTCTGCAGAACTGCACTTGCAAG

ACCATTATCAACTCCTAATCCCAGCTCAGAAAGGGAGCCTCTGCGACTCATTCATCGCCCTCCAGGACT

GACTGCATTGCACAGATGATGGATATTTACGTATGTTTGAAACGACCATCCTGGATGGTGGACAATAAA

AGAATGAGGACTGCTTCAAATTTCCAGTGGCTGTTATCAACATTTATTCTTCTATATCTAATGAATCAA

GTAAATAGCCAGAAAAAGGGGGCTCCTCATGATTTGAAGTGTGTAACTAACAATTTGCAAGTGTGGAAC

TGTTCTTGGAAAGCACCCTCTGGAACAGGCCGTGGTACTGATTATGAAGTTTGCATTGAAAACAGGTCC

CGTTCTTGTTATCAGTTGGAGAAAACCAGTATTAAAATTCCAGCTCTTTCACATGGTGATTATGAAATA

ACAATAAATTCTCTACATGATTTTGGAAGTTCTACAAGTAAATTCACACTAAATGAACAAAACGTTTCC

TTAATTCCAGATACTCCAGAGATCTTGAATTTGTCTGCTGATTTCTCAACCTCTACATTATACCTAAAG

TGGAACGACAGGGGTTCAGTTTTTCCACACCGCTCAAATGTTATCTGGGAAATTAAAGTTCTACGTAAA

GAGAGTATGGAGCTCGTAAAATTAGTGACCCACAACACAACTCTGAATGGCAAAGATACACTTCATCAC

TGGAGTTGGGCCTCAGATATGCCCTTGGAATGTGCCATTCATTTTGTGGAAATTAGATGCTACATTGAC

AATCTTCATTTTTCTGGTCTCGAAGAGTGGAGTGACTGGAGCCCTGTGAAGAACATTTCTTGGATACCT

GATTCTCAGACTAAGGTTTTTCCTCAAGATAAAGTGATACTTGTAGGCTCAGACATAACATTTTGTTGT

GTGAGTCAAGAAAAAGTGTTATCAGCACTGATTGGCCATACAAACTGCCCCTTGATCCATCTTGATGGG

GAAAATGTTGCAATCAAGATTCGTAATATTTCTGTTTCTGCAAGTAGTGGAACAAATGTAGTTTTTACA

ACCGAAGATAACATATTTGGAACCGTTATTTTTGCTGGATATCCACCAGATACTCCTCAACAACTGAAT

TGTGAGACACATGATTTAAAAGAAATTATATGTAGTTGGAATCCAGGAAGGGTGACAGCGTTGGTGGGC

CCACGTGCTACAAGCTACACTTTAGTTGAAAGTTTTTCAGGAAAATATGTTAGACTTAAAAGAGCTGAA

GCACCTACAAACGAAAGCTATCAATTATTATTTCAAATGCTTCCAAATCAAGAAATATATAATTTTACT

TTGAATGCTCACAATCCGCTGGGTCGATCACAATCAACAATTTTAGTTAATATAACTGAAAAAGTTTAT

CCCCATACTCCTACTTCATTCAAAGTGAAGGATATTAATTCAACAGCTGTTAAACTTTCTTGGCATTTA

CCAGGCAACTTTGCAAAGATTAATTTTTTATGTGAAATTGAAATTAAGAAATCTAATTCAGTACAAGAG

CAGCGGAATGTCACAATCAAAGGAGTAGAAAATTCAAGTTATCTTGTTGCTCTGGACAAGTTAAATCCA

TACACTCTATATACTTTTCGGATTCGTTGTTCTACTGAAACTTTCTGGAAATGGAGCAAATGGAGCAAT

AAAAAACAACATTTAACAACAGAAGCCAGTCCTTCAAAGGGGCCTGATACTTGGAGAGAGTGGAGTTCT

GATGGAAAAAATTTAATAATCTATTGGAAGCCTTTACCCATTAATGAAGCTAATGGAAAAATACTTTCC

TACAATGTATCGTGTTCATCAGATGAGGAAACACAGTCCCTTTCTGAAATCCCTGATCCTCAGCACAAA

GCAGAGATACGACTTGATAAGAATGACTACATCATCAGCGTAGTGGCTAAAAATTCTGTGGGCTCATCA

CCACCTTCCAAAATAGCGAGTATGGAAATTCCAAATGATGATCTCAAAATAGAACAAGTTGTTGGGATG

GGAAAGGGGATTCTCCTCACCTGGCATTACGACCCCAACATGACTTGCGACTACGTCATTAAGTGGTGT

AACTCGTCTCGGTCGGAACCATGCCTTATGGACTGGAGAAAAGTTCCCTCAAACAGCACTGAAACTGTA

ATAGAATCTGATGAGTTTCGACCAGGTATAAGATATAATTTTTTCCTGTATGGATGCAGAAATCAAGGA
TATCAATTATTACGCTCCATGATTGGATATATAGAAGAATTGGCTCCCATTGTTGCACCAAATTTTACT
GTTGAGGATACTTCTGCAGATTCGATATTAGTAAAATGGGAAGACATTCCTGTGGAAGAACTTAGAGGC
TTTTTAAGAGGATATTTGTTTTACTTTGGAAAAGGAGAAAGAGACACATCTAAGATGAGGGTTTTAGAA
TCAGGTCGTTCTGACATAAAAGTTAAGAATATTACTGACATATCCCAGAAGACACTGAGAATTGCTGAT
CTTCAAGGTAAAACAAGTTACCACCTGGTCTTGCGAGCCTATACAGATGGTGGAGTGGGCCCGGAGAAG
AGTATGTATGTGGTGACAAAGGAAAATTCTGTGGGATTAATTATTGCCATTCTCATCCCAGTGGCAGTG
GCTGTCATTGTTGGAGTGGTGACAAGTATCCTTTGCTATCGGAAACGAGAATGGATTAAAGAAACCTTC
TACCCTGATATTCCAAATCCAGAAAACTGTAAAGCATTACAGTTTCAAAAGAGTGTCTGTGAGGGAAGC
AGTGCTCTTAAAACATTGGAAATGAATCCTTGTACCCCAAATAATGTTGAGGTTCTGGAAACTCGATCA
GCATTTCCTAAAATAGAAGATACAGAAATAATTTCCCCAGTAGCTGAGCGTCCTGAAGATCGCTCTGAT
GCAGAGCCTGAAAACCATGTGGTTGTGTCCTATTGTCCACCCATCATTGAGGAAGAAATACCAAACCCA
GCCGCAGATGAAGCTGGAGGGACTGCACAGGTTATTTACATTGATGTTCAGTCGATGTATCAGCCTCAA
GCAAAACCAGAAGAAGAACAAGAAAATGACCCTGTAGGAGGGGCAGGCTATAAGCCACAGATGCACCTC
CCCATTAATTCTACTGTGGAAGATATAGCTGCAGAAGAGGACTTAGATAAAACTGCGGGTTACAGACCT
CAGGCCAATGTAAATACATGGAATTTAGTGTCTCCAGACTCTCCTAGATCCATAGACAGCAACAGTGAG
ATTGTCTCATTTGGAAGTCCATGCTCCATTAATTCCCGACAATTTTTGATTCCTCCTAAAGATGAAGAC
TCTCCTAAATCTAATGGAGGAGGGTGGTCCTTTACAAACTTTTTTCAGAACAAACCAAACGATTAACAG
TGTCACCGTGTCACTTCAGTCAGCCATCTCAATAAGCTCTTACTGCTAGTGTTGCTACATCAGCACTGG
GCATTCTTGGAGGGATCCTGTGAAGTATTGTTAGGAGGTGAACTTCACTACATGTTAAGTTACACTGAA
AGTTCATGTGCTTTTAATGTAGTCTAAAAGCCAAAGTATAGTGACTCAGAATCCTCAATCCACAAAACT
CAAGATTGGGAGCTCTTTGTGATCAAGCCAAAGAATTCTCATGTACTCTACCTTCAAGAAGCATTTCAA
GGCTAATACCTACTTGTACGTACATGTAAAACAAATCCCGCCGCAACTGTTTTCTGTTCTGTTGTTTGT
GGTTTTCTCATATGTATACTTGGTGGAATTGTAAGTGGATTTGCAGGCCAGGGAGAAAATGTCCAAGTA
ACAGGTGAAGTTTATTTGCCTGACGTTTACTCCTTTCTAGATGAAAACCAAGCACAGATTTTAAAACTT
CTAAGATTATTCTCCTCTATCCACAGCATTCACNNNNNNNNNNNNNNNNNNNNNNNNNNNGTAGTGACAGCGAT
TTAGTGTTTTGTTTGATAAAGTATGCTTATTTCTGTGCCTACTGTATAATGGTTATCAAACAGTTGTCT
CAGGGGTACAAACTTTGAAAACAAGTGTGACACTGACCAGCCCAAATCATAATCATGTTTTCTTGCTGT
GATAGGTTTTGCTTGCCTTTTCATTATTTTTTAGCTTTTATGCTTGCTTCCATTATTTCAGTTGGTTGC
CCTAATATTTAAAATTTACACTTCTAAGACTAGAGACCCACATTTTTTAAAAATCATTTTATTTTGTGA
TACAGTGACAGCTTTATATGAGCAAATTCAATATTATTCATAAGCATGTAATTCCAGTGACTTACTATG
TGAGATGACTACTAAGCAATATCTAGCAGCGTTAGTTCCATATAGTTCTGATTGGATTTCGTTCCTCCT
GAGGAGACCATGCCGTTGAGCTTGGCTACCCAGGCAGTGGTGATCTTTGACACCTTCTGGTGGATGTTC
CTCCCACTCATGAGTCTTTTCATCATGCCACATTATCTGATCCAGTCCTCACATTTTTAAATATAAAAC
TAAAGAGAGAATGCTTCTTACAGGAACAGTTACCCAAGGGCTGTTTCTTAGTAACTGTCATAAACTGAT
CTGGATCCATGGGCATACCTGTGTTCGAGGTGCAGCAATTGCTTGGTGAGCTGTGCAGAATTGATTGCC
TTCAGCACAGCATCCTCTGCCCACCCTTGTTTCTCATAAGCGATGTCTGGAGTGATTGTGGTTCTTGGA
AAAGCAGAAGGAAAAACTAAAAAGTGTATCTTGTATTTTCCCTGCCCTCAGGTTGCCTATGTATTTTAC
CTTTTCATATTTAAGGCAAAAGTACTTGAAAATTTTAAGTGTCCGAATAAGATATGTCTTTTTTGTTTG
TTTTTTTTGGTTGGTTGTTTGTTTTTTATCATCTGAGATTCTGTAATGTATTTGCAAATAATGGATCAA

TTAATTTTTTTTGAAGCTCATATTGTATCTTTTTAAAAACCATGTTGTGGAAAAAAGCCAGAGTGACAA
GTGACAAAATCTATTTAGGAACTCTGTGTATGAATCCTGATTTTAACTGCTAGGATTCAGCTAAATTTC
TGAGCTTTATGATCTGTGGAAATTTGGAATGAAATCGAATTCATTTTGTACATACATAGTATATTAAAA
CTATATAATAGTTCATAGAAATGTTCAGTAATGAAAAAATATATCCAATCAGAGCCATCCCGAAAAAAA
AAAAAAAA   (SEQ ID NO: 3102).

The length of this sequence was determined using batch, automated computational methods and the sequence, as sense strand, its length, and the desired location of the probe sequence near the 3' end of the mRNA was submitted to Array Designer Ver 1.1 (Premier Biosoft International, Palo Alto, CA). Search quality was set at 100%, number of best probes set at 1, length range set at 50 base pairs, Target Tm set at 75 C. degrees plus or minus 5 degrees, Hairpin max deltaG at 6.0 -kcal/mol., Self dimmer max deltaG at 6.0 -kcal/mol, Run/repeat (dinucleotide) max length set at 5, and Probe site minimum overlap set at 1. When none of the 49 possible probes met the criteria, the probe site would be moved 50 base pairs closer to the 5' end of the sequence and resubmitted to Array Designer for analysis. When no possible probes met the criteria, the variation on melting temperature was raised to plus and minus 8 degrees and the number of identical basepairs in a run increased to 6 so that a probe sequence was produced.

In the sequence above, using the criteria noted above, Array Designer Ver 1.1 designed a probe corresponding to oligonucleotide number 3037 and is indicated by underlining in the sequence above. It has a melting temperature of 68.4 degrees Celsius and a max run of 6 nucleotides and represents one of the cases where the criteria for probe design in Array Designer Ver 1.1 were relaxed in order to obtain an oligonucleotide near the 3' end of the mRNA (Low melting temperature was allowed).

Clone 463D12

Clone 463D12 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using the BLAST search tool. The sequence matched accession number AI184553, an EST sequence with the definition line "qd60a05.x1 Soares_testis_NHT Homo sapiens cDNA clone IMAGE:1733840 3' similar to gb:M29550 PROTEIN PHOSPHATASE 2B CATALYTIC SUBUNIT 1 (HUMAN):, mRNA sequence." The E value of the alignment was 1.00×10^{-118}. The GenBank sequence begins with a poly-T region, suggesting that it is the antisense strand, read 5' to 3'. The beginning of this sequence is complementary to the 3' end of the mRNA sense strand. The accession number for this sequence was included in a text file of accession numbers representing antisense sequences. Sequences for antisense strand mRNAs were obtained by uploading a text file containing desired accession numbers as an Entrez search query using the Batch Entrez web interface and saving the results locally as a FASTA file. The following sequence was obtained, and the region of alignment of clone 463D12 is outlined:

TTTTTTTTTTTTTTCTTAAATAGCATTTATTTTCTCTCAAAAAGCCTATTATGTACTAACAAGTGTTCC
TCTAAATTAGAAAGGCATCACTACTAAAATTTTATACATATTTTTTATATAAGAGAAGGAATATTGGGT
TACAATCTGAATTTCTCTTTATGATTTCTCTTAAAGTATAGAACAGCTATTAAAATGACTAATATTGCT
AAAATGAAGGCTACTAAATTTCCCCAAGAATTTCGGTGGAATGCCCAAAAATGGTGTTAAGATATGCAG
AAGGGCCCATTTCAAGCAAAGCAATCTCTCCACCCCTTCATAAAAGATTTAAGCTAAAAAAAAAAAAAA

AAGAA GAAAATCCAACAGCTGAAGACATTGGGCTATTTATAAATCTTCTCCCAGTCCCCCAGACAGCCT

CACATGGGGGCTGTAAACAGCTAACTAAAATATCTTTGAGACTCTTATGTCCACACCCACTGACACAAG

GAGAGCTGTAACCACAGTGAAACTAGACTTTGCTTTCCTTTAGCAAGTATGTGCCTATGATAGTAAACT

GGAGTAAATGTAACA GTAATAAAACAAATTTTTTTTAAAAATAAAAATTATACCTTTTTCTCCAACAAA

CGGTAAAGACCACGTGAAGACATCCATAAAATTAGGCAACCAGTAAAGATGTGGAGAACCAGTAAACTG

TCGAAATTCATCACATTATTTTCATACTTTAATACAGCAGCTTTAATTATTGGAGAACATCAAAGTAAT

TAGGTGCCGAAAAACATTGTTATTAATGAAGGGAACCCCTGACGTTTGACCTTTTCTGTACCATCTATA

GCCCTGGACTTGA   (SEQ ID NO: 3103)

The FASTA file, including the sequence of AA184553, was then masked using the RepeatMasker web
interface, as shown below. The region of alignment of clone 463D12 is outlined.

TTTTTTTTTTTTTTTCTTAAATAGCATTTATTTTCTCTCAAAAAGCCTATTATGTACTAACAAGTGTTCC

TCTAAATTAGAAAGGCATCACTACNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNGAGAAGGAATATTGGGT

TACAATCTGAATTTCTCTTTATGATTTCTCTTAAAGTATAGAACAGCTATTAAAATGACTAATAT<u>TGCT</u>

<u>AAAATGAAGGCTACTAAATTTCCCCAAGAATTTCGGTGGAATGCCC</u>AAAAATGGTGTTAAGATATGCAG

AAGGGCCCATTTCAAGCAAAGCAATCTCTCCACCCCTTCATAAAAGATTTAAGCTAAAAAAAAAAAAAA

AAGAA GAAAATCCAACAGCTGAAGACATTGGGCTATTTATAAATCTTCTCCCAGTCCCCCAGACAGCCT

CACATGGGGGCTGTAAACAGCTAACTAAAATATCTTTGAGACTCTTATGTCCACACCCACTGACACAAG

GAGAGCTGTAACCACAGTGAAACTAGACTTTGCTTTCCTTTAGCAAGTATGTGCCTATGATAGTAAACT

GGAGTAAATGTAACA GNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNCCTTTTTCTCCAACAAA

CGGTAAAGACCACGTGAAGACATCCATAAAATTAGGCAACCAGTAAAGATGTGGAGAACCAGTAAACTG

TCGAAATTCATCACATTATTTTCATACTTTAATACAGCAGCTTTAATTATTGGAGAACATCAAAGTAAT

TAGGTGCCGAAAAACATTGTTATTAATGAAGGGAACCCCTGACGTTTGACCTTTTCTGTACCATCTATA

GCCCTGGACTTGA   Masked version of 463D12 sequence. (SEQ ID NO:3104)

The sequence was submitted to Array Designer as described above, however, the desired location of
the probe was indicated at base pair 50 and if no probe met the criteria, moved in the 3' direction. The
complementary sequence from Array Designer was used, because the original sequence was antisense.
The oligonucleotide designed by Array Designer corresponds to oligonucleotide number 3054 and is
complementary to the underlined sequence above. The probe has a melting temperature of 72.7
degrees centigrade and a max run of 4 nucleotides.

Clone 72D4

Clone 72D4 was sequenced and compared to the nr, dbEST, and UniGene databases at NCBI using the
BLAST search tool. No significant matches were found in any of these databases. When compared to
the human genome draft, significant alignments were found to three consecutive regions of the
reference sequence NT_008060, as depicted below, suggesting that the insert contains three spliced
exons of an unidentified gene.

Residue numbers on clone 72D4 sequence	Matching residue numbers on NT_008060
1 – 198	478646 – 478843

197 – 489   479876 – 480168

491 – 585   489271 – 489365

Because the reference sequence contains introns and may represent either the coding or noncoding strand for this gene, BioCardia's own sequence file was used to design the oligonucleotide. Two complementary probes were designed to ensure that the sense strand was represented. The sequence of the insert in clone 72D4 is shown below, with the three putative exons outlined.

```
CAGGTCACACAGCACATCAGTGGCTACATGTGAGCTCAGACCTGGGTCTGCTGCTGTCTGT
CTTCCCAATATCCATGACCTTGACTGATGCAGGTGTCTAGGGATACGTCCATCCCCGTCCT
GCTGGAGCCCAGAGCACGGAAGCCTGGCCCTCCGAGGAGACAGAAGGGAGTGTCGGACA
CCATGACGAGAGCTTGGCAGAATAAATAACTTCTTTAAACAATTTTACGGCATGAAGAAA
TCTGGACCAGTTTATTAAATGGGATTTCTGCCACAAACCTTGGAAGAATCACATCATCTTA
NNCCCAAGTGAAAACTGTGTTGCGTAACAAAGAACATGACTGCGCTCCACACATACATCA
TTGCCCGGCGAGGCGGGACACAAGTCAACGACGGAACACTTGAGACAGGCCTACAACTG
TGCACGGGTCAGAAGCAAGTTTAAGCCATACTTGCTGCAGTGAGACTACATTTCTGTCTAT
AGAAGATACCTGACTTGATCTGTTTTTCAGCTCCAGTTCCCAGATGTGCGTGTTGTGGTCC
CCAAGTATCACCTTCCAATTTCTGGGAGCAGTGCTCTGGCCGGATCCTTGCCGCGCGGAT
AAAAAC  (SEQ ID NO: 3106)
```


The sequence was submitted to RepeatMasker, but no repetitive sequences were found. The sequence shown above was used to design the two 50-mer probes using Array Designer as described above. The probes are shown in bold typeface in the sequence depicted below. The probe in the sequence is oligonucleotide number 3020 (SEQ ID NO: 3020) and the complementary probe is oligonucleotide number 318 (SEQ ID NO:318). A portion of the target sequence is listed below (SEQ ID: 3106).


```
CAGGTCACACAGCACATCAGTGGCTACATGTGAGCTCAGACCTGGGTCTGCTGCTGTCTGTCTTCCCAA
TATCCATGACCTTGACTGATGCAGGTGTCTAGGGATACGTCCATCCCCGTCCTGCTGGAGCCCAGAGCA
CGGAAGCCTGGCCCTCCGAGGAGACAGAAGGGAGTGTCGGACACCATGACGAGAGCTTGGCAGAATAAA
TAACTTCTTTAAACAATTTTACGGCATGAAGAAATCTGGACCAGTTTATTAAATGGGATTTCTGCCACA
AACCTTGGAAGAATCACATCATCTTANNCCCAAGTGAAAACTGTGTTGCGTAACAAAGAACATGACTGC
GCTCCACACATACATCATTGCCCGGCGAGGCGGGACACAAGTCAACGACGGAACACTTGAGACAGGCCT
ACAACTGTGCACGGGTCAGAAGCAAGTTTAAGCCATACTTGCTGCAGTGAGACTACATTTCTGTCTATA
GAAGATACCTGACTTGATCTGTTTTTCAGCTCCAGTTCCCAGATGTGC
                                ←----GTCAAGGGTCTACACG
GTGTTGTGGTCCCCAAGTATCACCTTCCAATTTCTGGGAG--→
CACAACACCAGGGGTTCATAGTGGAAGGTTAAAG-5'


CAGTGCTCTGGCCGGATCCTTGCCGCGCGGATAAAAAACT---→
```

Confirmation of probe sequence

Following probe design, each probe sequence was confirmed by comparing the sequence against
dbEST, the UniGene cluster set, and the assembled human genome using BLASTn at NCBI.
Alignments, accession numbers, gi numbers, UniGene cluster numbers and names were examined and
the most common sequence used for the probe.

Example 9 - Production of an array of 8000 spotted 50mer oligonucleotides

We produced an array of *8000* spotted initial candidate 50mer oligonucleotides. Example 8
exemplifies the design and selection of probes for this array.

Sigma-Genosys (The Woodlands, TX) synthesized un-modified 50-mer oligonucleotides using
standard phosphoramidite chemistry, with a starting scale of synthesis of 0.05 μmole (see, e.g., R.
Meyers, ed. (1995) Molecular Biology and Biotechnology: A Comprehensive Desk Reference).
Briefly, to begin synthesis, a 3' hydroxyl nucleoside with a dimethoxytrityl (DMT) group at the 5' end
was attached to a solid support. The DMT group was removed with trichloroacetic acid (TCA) in order
to free the 5'-hydroxyl for the coupling reaction. Next, tetrazole and a phosphoramidite derivative of
the next nucleotide were added. The tetrazole protonates the nitrogen of the phosphoramidite, making
it susceptible to nucleophilic attack. The DMT group at the 5'-end of the hydroxyl group blocks
further addition of nucleotides in excess. Next, the inter-nucleotide linkage was converted to a
phosphotriester bond in an oxidation step using an oxidizing agent and water as the oxygen donor.
Excess nucleotides were filtered out and the cycle for the next nucleotide was started by the removal of
the DMT protecting group. Following the synthesis, the oligo was cleaved from the solid support. The
oligonucleotides were desalted, resuspended in water at a concentration of 100 or 200 μM, and placed
in 96-deep well format. The oligonucleotides were re-arrayed into Whatman Uniplate 384-well
polyproylene V bottom plates. The oligonucleotides were diluted to a final concentration 30 μM in 1X
Micro Spotting Solution Plus (Telechem/arrayit.com, Sunnyvale, CA) in a total volume of 15 μl. In
total, 8,031 oligonucleotides were arrayed into twenty-one 384-well plates.

Arrays were produced on Telechem/arrayit.com Super amine glass substrates (Telechem/arrayit.com),
which were manufactured in 0.1 mm filtered clean room with exact dimensions of 25x76x0.96 mm.
The arrays were printed using the Virtek Chipwriter with a Telechem 48 pin Micro Spotting Printhead.
The Printhead was loaded with 48 Stealth SMP3B TeleChem Micro Spotting Pins, which were used to
print oligonucleotides onto the slide with the spot size being 110-115 microns in diameter.

Example 10: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection

Genes were identified which have expression patterns useful for the diagnosis and monitoring of
cardiac allograft rejection. Further, sets of genes that work together in a diagnostic algorithm for

allograft rejection were identified. Patients, patient clinical data and patient samples used in the
discovery of markers below were derived from a clinical study described in example 5.

The collected clinical data is used to define patient or sample groups for correlation of expression data.
Patient groups are identified for comparison, for example, a patient group that possesses a useful or
interesting clinical distinction, verses a patient group that does not possess the distinction. Measures of
cardiac allograft rejection are derived from the clinical data described above to divide patients (and
patient samples) into groups with higher and lower rejection activity over some period of time or at any
one point in time. Such data are rejection grade as determined from pathologist reading of the cardiac
biopsies and data measuring progression of end-organ damage, including depressed left ventricular
dysfunction (decreased cardiac output, decreased ejection fraction, clinical signs of low cardiac output)
and usage of inotropic agents (Kobashigawa 1998).

Expression profiles correlating with occurrence of allograft rejection are identified, including
expression profiles corresponding to end-organ damage and progression of end-organ damage.
Expression profiles are identified predicting allograft rejection, and response to treatment or likelihood
of response to treatment. Subsets of the candidate library (or a previously identified diagnostic
nucleotide set) are identified, that have predictive value for the presence of allograft rejection or
prediction of allograft rejection or end organ damage.

Mononuclear RNA samples were collected from patients who had recently undergone a cardiac
allograft transplantation using the protocol described in example 2. The allograft rejection status at the
time of sample collection was determined by examination of cardiac biopsies as described in example
5.

180 samples were included in the analysis. Each patient sample was associated with a biopsy and
clinical data collected at the time of the sample. The cardiac biopsies were graded by a pathologist at
the local center and by a centralized pathologist who read the biopsy slides from all four local centers
in a blinded manner. Biopsy grades included 0, 1A, 1B, 2, 3A, and 3B. No grade 4 rejection was
identified. Dependent variables were developed based on these grades using either the local center
pathology reading or the higher of the two readings, local or centralized. The dependent variables used
for correlation of gene expression profiles with cardiac allograft rejection are shown in Table 4.
Dependent variables are used to create classes of samples corresponding to the presence or absence of
rejection.

Clinical data were also used to determine criteria for including samples in the analysis. The strictest
inclusion criteria required that samples be from patients who did not have a bacterial or viral infection,
were at least two weeks post cardiac transplant and were not currently admitted to the hospital. A
second inclusion criteria (inclusion 2) reduced the post-transplant criteria to 1 week and eliminated the
hospital admission criteria.

After preparation of RNA (example 2), amplification, labeling, hybridization, scanning, feature
extraction and data processing were done as described in Example 11, using the oligonucleotide
microarrays described in Example 9. The resulting log ratio of expression of Cy3 (patient sample)/
Cy5 (R50 reference RNA) was used for analysis. This dataset is called the "static" data. A second

type of dataset, referenced, was derived from the first. These datasets compared the gene expression log ratio in each sample to a baseline sample from the same patient using the formula:

$$\text{ref log ratio} = \left(\text{log ratio}_{sample}\right) - \left(\text{log ratio}_{baseline}\right)$$

Two referenced datasets were used, named "0 HG" and "Best 0". The baseline for 0 HG was a Grade 0 sample from the same patient as the sample, using the highest grade between the centralized and local pathologists. The baseline for Best 0 was a Grade 0 sample from the same patient as the sample, using both the local and centralized reader biopsy grade data. When possible a Grade 0 prior to the sample was used as the baseline in both referenced datasets.

The datasets were also divided into subsets to compare analysis between two subsets of roughly half of the data. The types of subsets constructed were as follows. First half/second half subsets were the first half of the samples and the second half of the samples from a dataset ordered by sample number. Odd/even subsets used the same source, a dataset ordered by sample number, but the odd subset consisted of every 2nd sample starting with the first and the even subset consisted of every 2nd sample starting with the second sample, Center 14/other subsets were the same datasets, divided by transplant hospital. The center 14 subset consisted of all samples from patients at center 14, while the other subset consisted of all samples from the other three centers (12,13, and 15).

Initially, significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to discover genes that were differentially expressed between the rejection and no-rejection groups. Ninety-six different combinations of dependent variables, inclusion criteria, static/referenced, and data subsets were used in SAM analysis to develop the primary lists of genes significantly differentially expressed between rejection and no-rejection. The most significant of these genes were chosen based on the following criteria. Tier 1 genes were those which appeared with an FDR of less than 20% in identical analyses in two independent subsets. Tier 2 genes were those which appeared in the top 20 genes on the list with an FDR less than 20% more than 50% of the time over all dependent variables with the inclusion criteria, and static/referenced constant. Tier 3 genes were those that appeared more than 50% of the time with an FDR less than 20% more than 50% of the time over all dependent variables with the inclusion criteria, and static/referenced constant. The genes that were identified by the analysis as statistically differentially expressed between rejection and no rejection are shown in Table 2.

SAM chooses genes as significantly different based on the magnitude of the difference between the groups and the variation among the samples within each group. An example of the difference between some Grade 0 and some Grade 3A samples for 9 genes is shown in Figure 7A.

Additionally, many of these same combinations were used in the Supervised Harvesting of Expression Trees (SHET, Hastie et al. 2001) algorithm (see example 15) to identify markers that the algorithm chose as the best to distinguish between the rejection and no rejection classes using a bias factor of 0.01. The top 20 or 30 terms were taken from the SHET output and among all comparisons in either the static or referenced data the results were grouped. Any gene found in the top 5 terms in more than 50% of the analyses was selected to be in group B1 (Table 2). The occurrences of each gene were tabulated over all SHET analysis (for either static or referenced data) and the 10 genes that occurred the most were selected to be in group B2 (Table 2).

An additional classification method used was CART (Salford Systems, San Diego, example 15). Either the static or referenced dataset was reduced to only the genes for which expression values (log ratios) were present in at least 80% of the samples. These data were used in CART with the default settings, using the Symmetric Gini algorithm. Each of the dependent variables was used with both the full sample set and the strict inclusion criteria. Two groups of genes were identified. Group C1 were those genes that were a primary splitter (1st decision node). Group C2 genes were the 10 genes that occurred as splitters the most often over all these analyses.

Two other classification models were developed and their best genes identified as markers of cardiac allograft rejection. Group D genes were identified from a set of 59 samples, referenced data, local biopsy reading grade, using logistic regression. Group E genes were identified from the primary static dataset using a K-nearest neighbor classification algorithm.

Both hierarchical clustering (Eisen et al. 1998) and CART were used to identify surrogates for each identified marker. Hierarchical clustering surrogates are genes co-expressed in these and were chosen from the nearest branches of the dendrogram. CART surrogates were identified by CART as the surrogates for those genes chosen as primary splitters at decision nodes.

Primers for real-time PCR validation were designed for each of the marker genes as described in Example 13.

CART was used to build a decision tree for classification of samples as rejection or no-rejection using the gene expression data from the arrays. The analysis identified sets of genes that can be used together to accurately identify samples derived from cardiac allograft transplant patients. The set of genes and the identified threshold expression levels for the decision tree are referred to as a "models". This model can be used to predict the rejection state of an unknown sample. The input data were the static expression data (log ratio) and the referenced expression data (log ratio referenced to the best available grade 0 from either the centralized reader or the local reader) for 139 of our top marker genes. These two types of expression data were entered into the CART software as independent variables. The dependent variable was rejection state, defined for this model as no rejection = grade 0 and rejection = grade 3A. Samples were eliminated from consideration in the training set if they were from patients with either bacterial or viral infection or were from patients who were less than two weeks post-transplant. The method used was Symmetric Gini, allowing linear combinations of independent variables. The costs were set to 1 for both false negatives and false positives and the priors were set equal for the two states. No penalties were assessed for missing data, however the marker genes selected have strong representation across the dataset. 10-fold cross validation was used to test the model. Settings not specified remained at the default values.

The model shown in Figure 7B is based on decisions about expression values at three nodes, each a different marker gene. The cost assigned to this model is 0.292, based on the priors being equal, the costs set to 1 for each type of error, and the results from the 10-fold cross validation.

In the training set, no rejection samples were misclassified (sensitivity = 100%) and only 1 no-rejection sample was misclassified (specificity = 94.4%). Following 10-fold cross validation, 2 rejection samples were misclassified (sensitivity = 87.5%) and 3 no-rejection samples were misclassified (specificity = 83.3%). The CART software assigns surrogate markers for each decision node.

These genes can be used alone or in association with other genes or variables to build a diagnostic gene set or a classification algorithm. These genes can be used in association with known gene markers for rejection (such as those identified in the prior art) to provide a diagnostic algorithm.

Example 11- Amplification, labeling, and hybridization of total RNA to an oligonucleotide microarray
Amplification, labeling, hybridization and scanning

Samples consisting of at least 0.5 to 2 µg of intact total RNA were further processed for array hybridization. When available, 2 µg of intact total RNA is used for amplification. Amplification and labeling of total RNA samples was performed in three successive enzymatic reactions. First, a single-stranded DNA copy of the RNA was made (hereinafter, "ss-cDNA"). Second, the ss-cDNA was used as a template for the complementary DNA strand, producing double-stranded cDNA (hereinafter, "ds-cDNA, or cDNA"). Third, linear amplification was performed by in vitro transcription from a bacterial T_7 promoter. During this step, fluorescent-conjugated nucleotides were incorporated into the amplified RNA (hereinafter, "aRNA").

The first strand cDNA was produced using the Invitrogen kit (Superscript II). The first strand cDNA was produced in a reaction composed of 50 mM Tris-HCl (pH 8.3), 75 mM KCl, and 3 mM $MgCl_2$ (1x First Strand Buffer, Invitrogen), 0.5 mM dGTP, 0.5 mM dATP, 0.5 mM dTTP, 0.5 mM dCTP, 10 mM DTT, 200 U reverse transcriptase (Superscript II, Invitrogen, #18064014), 15 U RNase inhibitor (RNAGuard, Amersham Pharmacia, #27-0815-01), 5 µM T7T24 primer
(5'-GGCCAGTGAATTGTAATACGACTCACTATAGGGAGGCGGTTTTTTTTTTTTTTTTTTTTTTTT TTT-3'), (SEQ ID NO:3105) and 0.5 to 2 µg of selected sample total RNA. Several purified, recombinant control mRNAs from the plant Arabidopsis thaliana were added to the reaction mixture: 2-20 pg of the following genes CAB, RCA, LTP4, NAC1, RCP1,XCP2, RBCL, LTP6, TIM, and PRKase (Stratagene, #252201, #252202, #252204, #252208, #252207, #252206, #252203, #252205, #252209, #252210 respectively). The control RNAs allow the estimate of copy numbers for individual mRNAs in the clinical sample because corresponding sense oligonucleotide probes for each of these plant genes are present on the microarray. The final reaction volume of 20 µl was incubated at 42°C for 90 min.

For synthesis of the second cDNA strand, DNA polymerase and RNase were added to the previous reaction, bringing the final volume to 150 µl. The previous contents were diluted and new substrates were added to a final concentration of 20 mM Tris-HCl (pH 7.0) (Fisher Scientific, Pittsburgh, PA #BP1756-100), 90 mMKCl (Teknova, Half Moon Bay, CA, #0313-500) , 4.6 mM $MgCl_2$ (Teknova, Half Moon Bay, CA, #0304-500), 10 mM$(NH_4)_2SO_4$ (Fisher Scientific #A702-500)(1x Second Strand buffer, Invitrogen), 0.266 mM dGTP, 0.266 mM dATP, 0.266 mM dTTP, 0.266 mM dCTP, 40 U *E. coli* DNA polymerase (Invitrogen, #18010-025), and 2 U RNaseH (Invitrogen, #18021-014). The second strand synthesis took place at 16°C for 150 minutes.

Following second-strand synthesis, the ds-cDNA was purified from the enzymes, dNTPs, and buffers before proceeding to amplification, using phenol-chloroform extraction followed by ethanol precipitation of the cDNA in the presence of glycogen.

Alternatively, a silica-gel column is used to purify the cDNA (e.g. Qiaquick PCR cleanup from Qiagen, #28104). The volume of the column purified cDNA was reduced by ethanol precipitation in the

presence of glycogen in which the cDNA was collected by centrifugation at >10,000 xg for 30 minutes, the supernatant is aspirated, and 150 µl of 70% ethanol, 30% water was added to wash the DNA pellet. Following centrifugation, the supernatant was removed, and residual ethanol was evaporated at room temperature. Alternatively, the volume of the column purified cDNA is reduce in a vacuum evaporator where the supernatant is reduce to a final volume of 7.4 µl.

Linear amplification of the cDNA was performed by in vitro transcription of the cDNA. The cDNA pellet from the step described above was resuspended in 7.4 µl of water, and in vitro transcription reaction buffer was added to a final volume of 20 µl containing 7.5 mM GTP, 7.5 mM ATP, 7.5 mM TTP, 2.25 mM CTP, 1.025 mM Cy3-conjugated CTP (Perkin Elmer; Boston, MA, #NEL-580), 1x reaction buffer (Ambion, Megascript Kit, Austin, TX and #1334) and 1 % T_7 polymerase enzyme mix (Ambion, Megascript Kit, Austin, TX and #1334). This reaction was incubated at 37°C overnight. Following in vitro transcription, the RNA was purified from the enzyme, buffers, and excess NTPs using the RNeasy kit from Qiagen (Valencia, CA; # 74106) as described in the vendor's protocol. A second elution step was performed and the two eluates were combined for a final volume of 60 µl. RNA is quantified using an Agilent 2100 bioanalyzer with the RNA 6000 nano LabChip.

Reference RNA was prepared as described above, except Cy5-CTP was incorporated instead of Cy3CTP. Reference RNA from five reactions, each reaction started with 2 ug total RNA, was pooled together and quantitated as described above.

Hybridization to an array

RNA was prepared for hybridization as follows: for an 18mmx55mm array, 20 µg of amplified RNA (aRNA) was combined with 20 µg of reference aRNA. The combined sample and reference aRNA was concentrated by evaporating the water to 10 µl in a vacuum evaporator. The sample was fragmented by heating the sample at 95°C for 30 minutes to fragment the RNA into 50-200 bp pieces.

Alternatively, the combined sample and reference aRNA was concentrated by evaporating the water to 5 µl in a vacuum evaporator. Five µl of 20 mM zinc acetate was added to the aRNA and the mix incubated at 60°C for 10 minutes. Following fragmentation, 40 µl of hybridization buffer was added to achieve final concentrations of 5×SSC and 0.20 %SDS with 0.1 µg/ul of Cot-1 DNA (Invitrogen) as a competitor DNA. The final hybridization mix was heated to 98°C, and then reduced to 50°C at 0.1°C per second.

Alternatively, formamide is included in the hybridization mixture to lower the hybridization temperature.

The hybridization mixture was applied to a pre-heated 65°C microarray, surface, covered with a glass coverslip (Corning, #2935-246), and placed on a pre-heated 65°C hybridization chamber (Telechem, AHC-10). 15 ul of 5xSSC was placed in each of the reservoir in the hybridization chamber and the chamber was sealed and placed in a water bath at 62°C for overnight (16-20 hrs). Following incubation, the slides were washed in 2×SSC, 0.1% SDS for five minutes at 30°C, then in 2×SSC for five minutes at 30°C, then in 2xSSC for another five minutes at 30°C, then in 0.2×SSC for two minutes

at room temperature. The arrays were spun at 1000×g for 2 minutes to dry them. The dry microarrays are then scanned by methods described above.

The microarrays were imaged on the Agilent (Palo Alto, CA) scanner G2565AA. The scan settings using the Agilent software were as follows: for the PMT Sensitivity (100% Red and 100% Green); Scan Resolution (10 microns); red and green dye channels; used the default scan region for all slides in the carousel; using the largest scan region; scan date for Instrument ID; and barcode for Slide ID. The full image produced by the Agilent scanner was flipped, rotated, and split into two images (one for each signal channel) using TIFFSplitter (Agilent, Palo Alto, CA). The two channels are the output at 532 nm (Cy3-labeled sample) and 633 nm (Cy5-labeled R50). The individual images were loaded into GenePix 3.0 (Axon Instruments, Union City, CA) for feature extraction, each image was assigned an excitation wavelength corresponding the file opened; Red equals 633 nm and Green equals 532 nm. The setting file (gal) was opened and the grid was laid onto the image so that each spot in the grid overlaped with >50% of the feature. Then the GenePix software was used to find the features without setting minimum threshold value for a feature. For features with low signal intensity, GenePix reports "not found". For all features, the diameter setting was adjusted to include only the feature if necessary.

The GenePix software determined the median pixel intensity for each feature (F_i) and the median pixel intensity of the local background for each feature (B_i) in both channels. The standard deviation (SDF_i and SDB_i) for each is also determined. Features for which GenePix could not discriminate the feature from the background were "flagged" as described below.

Following feature extraction into a " .gpr" file, the header information of the .gpr file was changed to carry accurate information into the database. An Excel macro was written to include the following information: Name of the original .tif image file, SlideID, Version of the feature extraction software, GenePix Array List file, GenePix Settings file, ScanID, Name of person who scanned the slide, Green PMT setting, Red PMT setting, ExtractID (date .gpr file was created, formatted as yyyy.mm.dd-hh.mm.ss), Results file name (same as the .gpr file name), StorageCD, and Extraction comments.

Pre-processing with Excel Templates

Following analysis of the image and extraction of the data, the data from each hybridization was pre-processed to extract data that was entered into the database and subsequently used for analysis. The complete GPR file produced by the feature extraction in GenePix was imported into an excel file pre-processing template or processed using a AWK script. Both programs used the same processing logic and produce identical results. The same excel template or AWK script was used to process each GPR file. The template performs a series of calculations on the data to differentiate poor features from others and to combine duplicate or triplicate feature data into a single data point for each probe.

The data columns used in the pre-processing were: Oligo ID, F633 Median (median value from all the pixels in the feature for the Cy5 dye), B633 Median (the median value of all the pixels in the local background of the selected feature for Cy5), B633 SD (the standard deviation of the values for the pixels in the local background of the selected feature for Cy5), F532 Median (median value from all the pixels in the feature for the Cy3 dye), B532 Median (the median value of all the pixels in the local background of the selected feature for Cy3), B532 SD (the standard deviation of the values for the pixels in the local background of the selected feature for Cy3), and Flags. The GenePix Flags column contains the flags set during feature extraction. "-75" indicates there were no features printed on the array in that position, "-50" indicates that GenePix could not differentiate the feature signal from the local background, and "-100" indicates that the user marked the feature as bad.

Once imported, the data associated with features with -75 flags was not used. Then the median of B633 SD and B532 SD were calculated over all features with a flag value of "0". The minimum values of B633 Median and B532 Median were identified, considering only those values associated with a flag value of "0". For each feature, the signal to noise ratio (S/N) was calculated for both dyes by taking the fluorescence signal minus the local background (BGSS) and dividing it by the standard deviation of the local background:

$$S/N = \frac{F_i - B_i}{SDB_i}$$

If the S/N was less than 3, then an adjusted background-subtracted signal was calculated as the fluorescence minus the minimum local background on the slide. An adjusted S/N was then calculated as the adjusted background subtracted signal divided by the median noise over all features for that channel. If the adjusted S/N was greater than three and the original S/N were less than three, a flag of 25 was set for the Cy5 channel, a flag of 23 was set for the Cy3 channel, and if both met these criteria, then a flag of 28 was set. If both the adjusted S/N and the original S/N were less than three, then a flag of 65 was set for Cy5, 63 set for Cy3, and 68 set if both dye channels had an adjusted S/N less than three. All signal to noise calculations, adjusted background-subtracted signal, and adjusted S/N were calculated for each dye channel. If the BGSS value was greater than or equal to 64000, a flag was set to indicate saturation; 55 for Cy5, 53 for Cy3, 58 for both.

The BGSS used for further calculations was the original BGSS if the original S/N was greater than or equal to three. If the original S/N ratio was less than three and the adjusted S/N ratio was greater than or equal to three, then the adjusted BGSS was used. If the adjusted S/N ratio was less than three, then the adjusted BGSS was used, but with knowledge of the flag status.

To facilitate comparison among arrays, the Cy3 and Cy5 data were scaled. The log of the ratio of Green/Red was determined for all features. The median log ratio value for good features (Flags 0, 23, 25, 28, 63) was determined. The feature values were scaled using the following formula:

Log_Scaled_Feature_Ratio = Log_Feature_Ratio – Median_Log_Ratio.

The flag setting for each feature was used to determine the expression ratio for each probe, a choice of one, two or three features. If all features had flag settings in the same category (categories=negatives,

0 to 28, 53-58, and 63-68), then the average of the three scaled, anti log feature ratios was calculated If the three features did not have flags in the same category, then the feature or features with the best quality flags were used (0>25>23>28>55>53>58>65>63>68). Features with negative flags were never used. When the best flags were two or three features in the same category, the anti log average was used. If a single feature had a better flag category than the other two then the anti log of that feature ratio was used.

Once the probe expression ratios were calculated from the one, two, or three features, the log of the scaled, averaged ratios was taken as described below and stored for use in analyzing the data. Whichever features were used to calculate the probe value, the flag from those features was carried forward and stored as the flag value for that probe. 2 different data sets can be used for analysis. Flagged data uses all values, including those with flags. Filtered data sets are created by removing flagged data from the set before analysis.

Example 12: Real-time PCR validation of array expression results

Leukocyte microarray gene expression was used to discover expression markers and diagnostic gene sets for clinical outcomes. It is desirable to validate the gene expression results for each gene using a more sensitive and quantitative technology such as real-time PCR. Further, it is possible for the diagnostic nucleotide sets to be implemented as a diagnostic test as a real-time PCR panel. Alternatively, the quantitative information provided by real-time PCR validation can be used to design a diagnostic test using any alternative quantitative or semi-quantitative gene expression technology. To validate the results of the microarray experiments we used real-time, or kinetic, PCR. In this type of experiment the amplification product is measured during the PCR reaction. This enables the researcher to observe the amplification before any reagent becomes rate limiting for amplification. In kinetic PCR the measurement is of C_T (threshold cycle) or C_P (crossing point). This measurement ($C_T=C_P$) is the point at which an amplification curve crosses a threshold fluorescence value. The threshold is set to a point within the area where all of the reactions were in their linear phase of amplification. When measuring C_T, a lower C_T value is indicative of a higher amount of starting material since an earlier cycle number means the threshold was crossed more quickly.

Several fluorescence methodologies are available to measure amplification product in real-time PCR. Taqman (Applied BioSystems, Foster City, CA) uses fluorescence resonance energy transfer (FRET) to inhibit signal from a probe until the probe is degraded by the sequence specific binding and Taq 3' exonuclease activity. Molecular Beacons (Stratagene, La Jolla, CA) also use FRET technology, whereby the fluorescence is measured when a hairpin structure is relaxed by the specific probe binding to the amplified DNA. The third commonly used chemistry is Sybr Green, a DNA-binding dye (Molecular Probes, Eugene, OR). The more amplified product that is produced, the higher the signal. The Sybr Green method is sensitive to non-specific amplification products, increasing the importance of primer design and selection. Other detection chemistries can also been used, such as ethedium bromide or other DNA-binding dyes and many modifications of the fluorescent dye/quencher dye Taqman chemistry.

<u>Sample prep and cDNA synthesis</u>

The inputs for real time PCR reaction are gene-specific primers, cDNA from specific patient samples, and standard reagents. The cDNA was produced from mononuclear RNA (prepared as in example 2) or whole blood RNA by reverse transcription using Oligo dT primers (Invitrogen, 18418-012) and random hexamers (Invitrogen, 48190-011) at a final concentration of 0.5ng/µl and 3ng/µl respectively. For the first strand reaction mix, 0.5 µg of mononuclear total RNA or 2 µg of whole blood RNA and 1 µl of the Oligo dT/ Random Hexamer Mix, were added to water to a final volume of 11.5 µl. The sample mix was then placed at 70°C for 10 minutes. Following the 70°C incubation, the samples were chilled on ice, spun down, and 88.5 µl of first strand buffer mix dispensed into the reaction tube. The final first strand buffer mix produced final concentrations of 1X first strand buffer (Invitrogen, Y00146, Carlsbad, CA), 10 mM DTT (Invitrogen, Y00147), 0.5 mM dATP (NEB, N0440S, Beverly, MA), 0.5 mM dGTP (NEB, N0442S), 0.5mM dTTP (NEB, N0443S), 0.5 mM dCTP (NEB, N0441S), 200U of reverse transcriptase (Superscript II, Invitrogen, 18064-014), and 18U of RNase inhibitor (RNAGaurd Amersham Pharmacia, 27-0815-01, Piscataway, NJ). The reaction was incubated at 42°C for 90 minutes. After incubation the enzyme was heat inactivated at 70°C for 15 minutes, 2 U of RNAse H added to the reaction tube, and incubated at 37°C for 20 minutes.

<u>PRIMER DESIGN</u>

Two methods were used to design primers. The first was to use the software, Primer Express[tm] and recommendations for primer design that are provided with the GeneAmp® 7700 Sequence Detection System supplied by Applied BioSystems (Foster City, CA). The second method used to design primers was the PRIMER3 ver 0.9 program that is available from the Whitehead Research Institute, Cambridge, Massachusetts at the Whitehead Research web site. The program can also be accessed on the World Wide Web at the web site at the Massachusetts Institute of Technology website. Primers and Taqman/hybridization probes were designed as described below using both programs.

The Primer Express literature explains that primers should be designed with a melting temperature between 58 and 60 degrees C. while the Taqman probes should have a melting temperature of 68 to 70 under the salt conditions of the supplied reagents. The salt concentration is fixed in the software. Primers should be between 15 and 30 basepairs long. The primers should produce and amplicon in size between 50 and 150 base pairs, have a C-G content between 20% and 80%, have no more than 4 identical base pairs next to one another, and no more than 2 C's and G's in the last 5 bases of the 3' end. The probe cannot have a G on the 5' end and the strand with the fewest G's should be used for the probe.

Primer3 has a large number of parameters. The defaults were used for all except for melting temperature and the optimal size of the amplicon was set at 100 bases. One of the most critical is salt concentration as it affects the melting temperature of the probes and primers. In order to produce , primers and probes with melting temperatures equivalent to Primer Express, a number of primers and probes designed by Primer Express were examined using PRIMER3. Using a salt concentration of 50 mM these primers had an average melting temperature of 3.7 degrees higher than predicted by Primer

Express. In order to design primers and probes with equivalent melting temperatures as Primer Express using PRIMER3, a melting temperature of 62.7 plus/minus 1.0 degree was used in PRIMER3 for primers and 72.7 plus/minus 1.0 degrees for probes with a salt concentration of 50 mM.

The C source code for Primer3 was downloaded and complied on a Sun Enterprise 250 server using the GCC complier. The program was then used from the command line using a input file that contained the sequence for which we wanted to design primers and probes along with the input parameters as described by help files that accompany the software. Using scripting it was possible to input a number of sequences and automatically generate a number of possible probes and primers.

Primers for β-Actin (Beta Actin, Genbank Locus: NM_001101)and β-GUS: glucuronidase, beta, (GUSB, Genbank Locus: NM_000181), two reference genes, were designed using both methods and are shown here as examples:

The first step was to mask out repetitive sequences found in the mRNA sequences using RepeatMasker program that can be accessed at: the web site University of Washington Genome Repeatmasker website. (Smit, A.F.A. & Green, P.).

The last 500 basepairs on the last 3' end of masked sequence was then submitted to PRIMER3 using the following exemplary input sequences:

```
PRIMER_SEQUENCE_ID=>ACTB Beta Actin (SEQID 3083)
SEQUENCE=TTGGCTTGACTCAGGATTTAAAAACTGGAACGGTGAAGGTGACAGCAGTCGGTTGGACGA
GCATCCCCCAAAGTTCACAATGTGGCCGAGGACTTTGATTGCACATTGTTGTTTTTTAATAGTCATTCC
AAATATGAGATGCATTGTTACAGGAAGTCCCTTGCCATCCTAAAAGCACCCCACTTCTCTCTAAGGAGA
ATGGCCCAGTCCTCTCCCAAGTCCACACAGGGGAGGGATAGCATTGCTTTCGTGTAAATTATGTAATGC
AAAATTTTTTTAATCTTCGCCTTAATCTTTTTTATTTTGTTTTATTTTGAATGATGAGCCTTCGTGCCC
CCCCTTCCCCCTTTTTTCCCCCAACTTGAGATGTATGAAGGCTTTTGGTCTCCCTGGGAGTGGGTGGAG
GCAGCCGGGCTTACCTGTACACTGACTTGAGACCAGTTGAATAAAAGTGCACACCTTA
```

```
PRIMER_SEQUENCE_ID=>GUSB (SEQID 3084)
SEQUENCE=GAAGAGTACCAGAAAAGTCTGCTAGAGCAGTACCATCTGGGTCTGGATCAAAAACGCAGA
AAATATGTGGTTGGAGAGCTCATTTGGAATTTTGCCGATTTCATGACTGAACAGTCACCGACGAGAGTG
CTGGGGAATAAAAAGGGGATCTTCACTCGGCAGAGACAACCAAAAAGTGCAGCGTTCCTTTTGCGAGAG
AGATACTGGAAGATTGCCAATGAAACCAGGTATCCCCACTCAGTAGCCAAGTCACAATGTTTGGAAAAC
AGCCCGTTTACTTGAGCAAGACTGATACCACCTGCGTGTCCCTTCCTCCCCGAGTCAGGGCGACTTCCA
CAGCAGCAGAACAAGTGCCTCCTGGACTGTTCACGGCAGACCAGAACGTTTCTGGCCTGGGTTTTGTGG
TCATCTATTCTAGCAGGGAACACTAAAGGTGGAAATAAAAGATTTTCTATTATGGAAATAAAGAGTTGG
CATGAAAGTCGCTACTG
```

After running PRIMER3, 100 sets of primers and probes were generated for ACTB and GUSB. From this set, nested primers were chosen based on whether both left primers could be paired with both right primers and a single Taqman probe could be used on an insert of the correct size. With more experience we have decided not use the mix and match approach to primer selection and just use several of the top pairs of predicted primers.

```
For ACTB this turned out to be:
Forward 75 CACAATGTGGCCGAGGACTT(SEQID 3085),
Forward 80 TGTGGCCGAGGACTTTGATT(SEQID 3086),
Reverse 178 TGGCTTTTAGGATGGCAAGG(SEQID 3087), and
Reverse 168 GGGGGCTTAGTTTGCTTCCT(SEQID 3088).
```

Upon testing, the F75 and R178 pair worked best.

For GUSB the following primers were chosen:
Forward 59 AAGTGCAGCGTTCCTTTTGC(SEQID 3089),
Forward 65 AGCGTTCCTTTTGCGAGAGA (SEQID 3090),   ...
Reverse 158 CGGGCTGTTTTCCAAACATT (SEQID 3091), and
Reverse 197 GAAGGGACACGCAGGTGGTA (SEQID 3092).

No combination of these GUSB pairs worked well.

In addition to the primer pairs above, Primer Express predicted the following primers for GUSB:

Forward 178 TACCACCTGCGTGTCCCTTC (SEQID 3093) and Reverse 242

GAGGCACTTGTTCTGCTGCTG (SEQID 3094). This pair of primers worked to amplify the GUSB

mRNA.

The parameters used to predict these primers in Primer Express were:
Primer Tm: min 58, Max=60, opt 59, max difference=2 degrees
Primer GC: min=20% Max =80% no 3' G/C clamp
Primer: Length: min=9 max=40 opt=20
Amplicon: min Tm=0   max Tm=85
min = 50 bp max = 150 bp
Probe: Tm 10 degrees > primers, do not begin with a G on 5' end
Other: max base pair repeat = 3
max number of ambiguous residues = 0
secondary structure: max consecutive bp = 4, max total bp = 8
Uniqueness: max consecutive match = 9
max % match = 75
max 3' consecutive match = 7

Granzyme B is a marker of transplant rejection.

For Granzyme B the following sequence (NM_004131) (SEQID 3096) was used as input for Primer3 :

GGGGACTCTGGAGGCCCTCTTGTGTGTAACAAGGTGGCCCAGGGCATTGT
CTCCTATGGACGAAACAATGGCATGCCTCCACGAGCCTGCACCAAAGTCT
CAAGCTTTGTACACTGGATAAAGAAAACCATGAAACGCTACTAACTACAG
GAAGCAAACTAAGCCCCCGCTGTAATGAAACACCTTCTCTGGAGCCAAGT
CCAGATTTACACTGGGAGAGGTGCCAGCAACTGAATAAATACCTCTCCCA
GTGTAAATCTGGAGCCAAGTCCAGATTTACACTGGGAGAGGTGCCAGCAA
CTGAATAAATACCTCTTAGCTGAGTGG

For Granzyme B the following primers were chosen for testing:
Forward 81 ACGAGCCTGCACCAAAGTCT (SEQID 3097)
Forward 63 AAACAATGGCATGCCTCCAC (SEQID 3098)
Reverse 178 TCATTACAGCGGGGGCTTAG (SEQID 3099)
Reverse 168 GGGGGCTTAGTTTGCTTCCT (SEQID 3100)

Testing demonstrated that F81 and R178 worked well. .

Using this approach, primers were designed for all the genes that were shown to have expression

patterns that correlated with allograft rejection. These primer pairs are shown in Table 2, Table 8, and

are added to the sequence listing. Primers can be designed from any region of a target gene using this

approach.

PRIMER ENDPOINT TESTING

Primers were first tested to examine whether they would produce the correct size product without non-specific amplification. The standard real-time PCR protocol was used without the Rox and Sybr green dyes. Each primer pair was tested on cDNA made from universal mononuclear leukocyte reference RNA that was produced from 50 individuals as described in Example 3 (R50).

The PCR reaction consisted of 1X RealTime PCR Buffer (Ambion, Austin, TX), 2mM MgCl2 (Applied BioSystems, B02953), 0.2mM dATP (NEB), 0.2mM dTTP (NEB), 0.2mM dCTP (NEB), 0.2mM dGTP (NEB), .625U AmpliTaq Gold (Applied BioSystems, Foster City, CA), 0.3µM of each primer to be used (Sigma Genosys, The Woodlands, TX), 5µl of the R50 reverse-transcription reaction and water to a final volume of 19µl.

Following 40 cycles of PCR, 10 microliters of each product was combined with Sybr green at a final dilution of 1:72,000. Melt curves for each PCR product were determined on an ABI 7900 (Applied BioSystems, Foster City, CA), and primer pairs yielding a product with one clean peak were chosen for further analysis. One microliter of the product from these primer pairs was examined by agarose gel electrophoresis on an Agilent Bioanalyzer, DNA1000 chip (Palo Alto, CA). Results for 2 genes are shown in Figure 9. From the primer design and the sequence of the target gene, one can calculate the expected size of the amplified DNA product. Only primer pairs with amplification of the desired product and minimal amplification of contaminants were used for real-time PCR. Primers that produced multiple products of different sizes are likely not specific for the gene of interest and may amplify multiple genes or chromosomal loci.

PRIMER OPTIMIZATION/EFFICIENCY

Once primers passed the end-point PCR, the primers were tested to determine the efficiency of the reaction in a real-time PCR reaction. cDNA was synthesized from starting total RNA as described above. A set of 5 serial dilutions of the R50 reverse-transcribed cDNA (as described above) were made in water: 1:10, 1:20, 1:40, 1:80, and 1:160.

The Sybr Green real-time PCR reaction was performed using the Taqman PCR Reagent kit (Applied BioSystems, Foster City, CA, N808-0228). A master mix was made that consisted of all reagents except the primes and template. The final concentration of all ingredients in the reaction was 1X Taqman Buffer A (Applied BioSystems), 2mM MgCl2 (Applied BioSystems), 200µM dATP (Applied BioSystems), 200µM dCTP (Applied BioSystems), 200µM dGTP (Applied BioSystems), 400µM dUTP (Applied BioSystems), 1:400,000 diluted Sybr Green dye (Molecular Probes), 1.25U AmpliTaq Gold (Applied BioSystems). The PCR master mix was dispensed into two, light-tight tubes. Each β-Actin primer F75 and R178 (Sigma-Genosys, The Woodlands, TX), was added to one tube of PCR master mix and Each β-GUS primer F178 and R242 (Sigma-Genosys), was added to the other tube of PCR master mix to a final primer concentration of 300nM. 45µl of the β-Actin or β-GUS master mix was dispensed into wells, in a 96-well plate (Applied BioSystems). 5µl of the template dilution series was dispensed into triplicate wells for each primer. The reaction was run on an ABI 7900 Sequence Detection System (Applied BioSystems) with the following conditions: 10 min. at 95°C; 40 cycles of

95°C for 15 sec, 60°C for 1 min; followed by a disassociation curve starting at 50°C and ending at 95°C. .

The Sequence Detection System v2.0 software was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed the majority of the amplification curves to cross the threshold during the linear phase of amplification. The disassociation curve for each well was compared to other wells for that marker. This comparison allowed identification of "bad" wells, those that did not amplify, that amplified the wrong size product, or that amplified multiple products. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T values for triplicate wells were averaged. The data were plotted as a function of the $\log_{10}$ of the calculated starting concentration of RNA. The starting RNA concentration for each cDNA dilution was determined based on the original amount of RNA used in the RT reaction, the dilution of the RT reaction, and the amount used (5 µl) in the real-time PCR reaction. For each gene, a linear regression line was plotted through all of the dilutions series points. The slope of the line was used to calculate the efficiency of the reaction for each primer set using the equation:

$$E = 10^{\left(-\frac{1}{slope}\right)} - 1$$

Using this equation (Pfaffl 2001, Applied Biosystems User Bulletin #2), the efficiency for these β-actin primers is 1.28 and the efficiency for these β-GUS primers is 1.14 (Figure 10). This efficiency was used when comparing the expression levels among multiple genes and multiple samples. This same method was used to calculate reaction efficiency for primer pairs for each gene studied. A primer pair was considered successful if the efficiency was reproducibly determined to be between 0.7 and 2.4.

SYBR-GREEN ASSAYS

Once markers passed the Primer Efficiency QPCR (as stated above), they were used in real-time PCR assays. Patient RNA samples were reverse-transcribed to cDNA (as described above) and 1:10 dilutions made in water. In addition to the patient samples, a no template control (NTC) and a pooled reference RNA (see example 3) described in were included on every plate.

The Sybr Green real-time PCR reaction was performed using the Taqman Core PCR Reagent kit (Applied BioSystems, Foster City, CA, N808-0228). A master mix was made that consisted of all reagents except the primers and template. The final concentration of all ingredients in the reaction was 1X Taqman Buffer A (Applied BioSystems), 2mM MgCl2 (Applied BioSystems), 200µM dATP (Applied BioSystems), 200µM dCTP (Applied BioSystems), 200µM dGTP (Applied BioSystems), 400µM dUTP (Applied BioSystems), 1:400,000 diluted Sybr Green dye (Molecular Probes), 1.25U AmpliTaq Gold (Applied BioSystems). The PCR master mix was aliquotted into eight light-tight tubes, one for each marker to be examined across a set of samples. The optimized primer pair for each marker was then added to the PCR master mix to a final primer concentration of 300nM. 18µl of the each marker master mix was dispensed into wells in a 384well plate (Applied BioSystems). 2µl of the

1:10 diluted control or patient cDNA sample was dispensed into triplicate wells for each primer pair. The reaction was run on an ABI 7900 Sequence Detection System (Applied BioSystems) using the cycling conditions described above.

The Sequence Detection System v2.0 software (Applied BioSystems) was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed the majority of the amplification curves to cross the threshold during the linear phase of amplification. The disassociation curve for each well was compared to other wells for that marker. This comparison allowed identification of "bad" wells, those that did not amplify, that amplified the wrong size product, or that amplified multiple products. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T value representing any well identified as bad by analysis of disassociation curves was deleted. The C_T values for triplicate wells were averaged. A standard deviation (Stdev) and a coefficient of variation (CV) were calculated for the triplicate wells. If the CV was greater than 2, an outlier among the three wells was identified and deleted. Then the average was re-calculated. In each plate, ΔC_T was calculated for each marker-control combination by subtracting the average C_T of the target marker from the average C_T of the control (β-Actin or β-GUS). The expression relative to the control marker was calculated by taking two to the power of the ΔC_T of the target marker. For example, expression relative to β-Actin was calculated by the equation:

$$ErA = 2^{\left(C_{T,Actin} - C_{T,target}\right)}$$

All plates were run in duplicate and analyzed in the same manner. The percent variation was determined for each sample-marker combination (relative expression) by taking the absolute value of the value of the RE for the second plate from the RE for the first plate, and dividing that by the average. If more than 25% of the variation calculations on a plate are greater than 50%, then a third plate was run.

TAQMAN PROTOCOL

Real-time PCR assays were also done using Taqman PCR chemistry.

The Taqman real-time PCR reaction was performed using the Taqman Universal PCR Master Mix (Applied BioSystems, Foster City, CA, #4324018). The master mix was aliquoted into eight, light-tight tubes, one for each marker. The optimized primer pair for each marker was then added to the correctly labeled tube of PCR master mix. A FAM/TAMRA dual-labeled Taqman probe (Biosearch Technologies, Navoto, CA, DLO-FT-2) was then added to the correctly labeled tube of PCR master mix. Alternatively, different combinations of fluorescent reporter dyes and quenchers can be used such that the absorption wavelength for the quencher matches the emission wavelength for the reporter, as shown in Table 5. 18μl of the each marker master mix was dispensed into a 384well plate (Applied BioSystems). 2μl of the template sample was dispensed into triplicate wells for each primer pair. The final concentration of each reagent was: 1X TaqMan Universal PCR Master Mix, 300nM each primer, 0.25nM probe, 2μl 1:10 diluted template. The reaction was run on an ABI 7900 Sequence Detection

System (Applied Biosystems) using standard conditions (95°C for 10 min., 40 cycles of 95°C for 15 sec, 60°C for 1 min.).

The Sequence Detector v2.0 software (Applied BioSystems) was used to analyze the fluorescent signal from each well. The high end of the baseline was adjusted to between 8 and 20 cycles to reduce the impact on any data curves, yet be as high as possible to reduce baseline drift. A threshold value was selected that allowed most of the amplification curves to cross the threshold during the linear phase of amplification. The cycle number at which each amplification curve crossed the threshold (C_T) was recorded and the file transferred to MS Excel for further analysis. The C_T values for triplicate wells were averaged. The C_T values for triplicate wells were averaged. A standard deviation (Stdev) and a coefficient of variation (CV) were calculated for the triplicate wells. If the CV was greater than 2, an outlier among the three wells was identified and deleted. Then the average was re-calculated. In each plate, ΔC_T was calculated for each marker-control combination by subtracting the average C_T of the target marker from the average C_T of the control (β-Actin or β-GUS). The expression relative to the control marker was calculated by taking two to the power of the ΔC_T of the target marker. All plates were run in duplicate and analyzed in the same manner. The percent variation was determined for each sample-marker combination (relative expression) by taking the absolute value of the value of the RE for the second plate from the RE for the first plate, and dividing that by the average. If more than 25% of the variation calculations on a plate are greater than 50%, then a third plate was run.

BI-PLEXING

Variation of real-time PCR assays can arise from unequal amounts of RNA starting material between reactions. In some assays, to reduce variation, the control gene amplification was included in the same reaction well as the target gene. To differentiate the signal from the two genes, different fluorescent dyes were used for the control gene. β-Actin was used as the control gene and the TaqMan probe used was labeled with the fluorescent dye VIC and the quencher TAMRA (Biosearch Technologies, Navoto, CA, DLO-FT-2). Alternatively, other combinations of fluorescent reporter dyes and quenchers (Table 5) can be used as long as the emission wavelength of the reporter for the control gene is sufficiently different from the wavelength of the reporter dye used for the target. The control gene primers and probe were used at limiting concentrations in the reaction (150 nM primers and 0.125 nM probe) to ensure that there were enough reagents to amplify the target marker. The plates were run under the same protocol and the data are analyzed in the same way, but with a separate baseline and threshold for the VIC signal. Outliers were removed as above from both the FAM and VIC signal channels. The expression relative to control was calculated as above, using the VIC signal from the control gene.

ABSOLUTE QUANTITATION

Instead of calculating the expression relative to a reference marker, an absolute quantitation can be performed using real-time PCR. To determine the absolute quantity of each marker, a standard curve is constructed using serial dilutions from a known amount of template for each marker on the plate. The standard curve may be made using cloned genes purified from bacteria or using synthetic

complimentary oligonucleotides. In either case, a dilution series that covers the expected range of expression is used as template in a series of wells in the plate. From the average C_T values for these known amounts of template a standard curve can be plotted. From this curve the C_T values for the unknowns are used to identify the starting concentration of cDNA. These absolute quantities can be compared between disease classes (i.e. rejection vs. no-rejection) or can be taken as expression relative to a control gene to correct for variation among samples in sample collection, RNA purification and quantification, cDNA synthesis, and the PCR amplification.

CELL TYPE SPECIFIC EXPRESSION

Some markers are expressed only in specific types of cells. These markers may be useful markers for differentiation of rejection samples from no-rejection samples or may be used to identify differential expression of other markers in a single cell type. A specific marker for cytotoxic T-lymphocytes (such as CD8) can be used to identify differences in cell proportions in the sample. Other markers that are known to be expressed in this cell type can be compared to the level of CD8 to indicate differential gene expression within CD8 T-cells.

Control genes for PCR
As discussed above, PCR expression measurements can be made as either absolute quantification of gene expression using a standard curve or relative expression of a gene of interest compared to a control gene. In the latter case, the gene of interest and the control gene are measured in the same sample. This can be done in separate reactions or in the same reaction (biplex format, see above). In either case, the final measurement for expression of a gene is expressed as a ratio of gene expression to control gene expression. It is important for a control gene to be constitutively expressed in the target tissue of interest and have minimal variation in expression on a per cell basis between individuals or between samples derived from an individual. If the gene has this type of expression behavior, the relative expression ratio will help correct for variability in the amount of sample RNA used in an assay. In addition, an ideal control gene has a high level of expression in the sample of interest compared to the genes being assayed. This is important if the gene of interest and control gene are used in a biplex format. The assay is set up so that the control gene reaches its threshold Ct value early and its amplification is limited by primers so that it does not compete for limiting reagents with the gene of interest.
To identify an ideal control gene for an assay, a number of genes were tested for variability between samples and expression in both mononuclear RNA samples and whole blood RNA samples using the RNA procurement and preparation methods and real-time PCR assays described above. 6 whole-blood and 6 mononuclear RNA samples from transplant recipients were tested. The intensity levels and variability of each gene in duplicate experiments on both sample types are shown in Figure 11. Based on criteria of low variability and high expression across samples, β-actin, 18s, GAPDH, b2microglobulin were found to be good examples of control genes for the PAX samples. A single control gene may be incorporated as an internal biplex control is assays.

Controlling for variation in real time PCR

Due to differences in reagents, experimenters, and preparation methods, and the variability of pipetting steps, there is significant plate-to-plate variation in real-time PCR experiments. This variation can be reduced by automation (to reduce variability and error), reagent lot quality control, and optimal data handling. However, the results on replicate plates are still likely to be different since they are run in the machine at different times.

Variation can also enter in data extraction and analysis. Real-time PCR results are measured as the time (measured in PCR cycles) at which the fluorescence intensity ($\Box$Rn in Applied Biosystems SDS v2.1 software) crosses a user-determined threshold (CT). When performing relative quantification, the CT value for the target gene is subtracted from the CT value for a control gene. This difference, called ΔCT, is the value compared among experiments to determine whether there is a difference between samples. Variation in setting the threshold can introduce additional error. This is especially true in the duplexed experimental format, where both the target gene and the control gene are measured in the same reaction tube. Duplexing is performed using dyes specific to each of the two genes. Since two different fluorescent dyes are used on the plate, two different thresholds are set. Both of these thresholds contribute to each ΔCT. Slight differences in the each dye's threshold settings (relative to the other dye) from one plate to the next can have significant effects on the ΔCT.

There are several methods for setting the threshold for a PCR plate. Older versions of SDS software (Applied Biosystems) determine the average baseline fluorescence for the plate and the standard deviation of the baseline. The threshold is set to 10x the standard deviation of the baseline. In SDS 2.0 the users must set the baseline by themselves. Software from other machine manufacturers either requires the user to set the threshold themselves or uses different algorithms. The latest version of the SDS software (SDS 2.1) contains Automatic baseline and threshold setting. The software sets the baseline separately for each well on the plate using the ΔRn at cycles preceding detectable levels. Variability among plates is dependent on reproducible threshold setting. This requires a mathematical or experimental data driven threshold setting protocol. Reproducibly setting the threshold according to a standard formula will minimize variation that might be introduced in the threshold setting process. Additionally, there may be experimental variation among plates that can be reduced by setting the threshold to a component of the data. We have developed a system that uses a set of reactions on each plate that are called the threshold calibrator (TCb). The TCb wells are used to set the threshold on all plates.

1. The TCb wells contain a template, primers, and probes that are common among all plates within an experiment.

2. The threshold is set within the minimum threshold and maximum threshold determined above.

3. The threshold is set to a value in this range that results in the average CT value for the TCb wells to be the same on all plates.

These methods were used to derive the primers depicted in Table 2C.

Example 13: Real-time PCR expression markers of acute allograft rejection

In examples 14 and 16, genes were identified as useful markers of cardiac and renal allograft rejection using microarrays. Some genes identified through these studies are listed in Table 2. In order to validate these findings, obtain a more precise measurement of expression levels and develop PCR reagents for diagnostic testing, real-time PCR assays were performed on samples from allograft recipients using primers to the identified genes. Some gene specific PCR primers were developed and tested for all genes in Table 2A as described in example 12. Some primers are listed in Table 2C and the sequence listing. These primers were used to measure expression of the genes relative to β-actin or β-gus in 69 mononuclear RNA samples obtained from cardiac allograft recipients using Sybr green real-time PCR assays as described in example 12. Each sample was associated with an ISHLT cardiac rejection biopsy grade. The samples were tested in 2 phases. In phase I, 14 Grade 0, 1 Grade 1A, 3 Grade 2 and 9 Grade 3A samples were tested. In phase II, 19 Grade 2, 4 Grade 1B, 4 Grade 2 and 15 Grade 3A samples were tested. Data was analyzed for each phase individually and for the combined phase I + II sample set. These data are summarized in Table 6.

The average fold change in expression between rejection (3A) and no rejection (0) samples was calculated. A t-test was done to determine the significance with which each gene was differentially expressed between rejection and no rejection and a p-value was calculated. Genes with high average fold changes and low p-values are considered best candidates for further development as rejection markers. However, it is important to note that a gene with a low average fold change and a high p-value may still be a useful marker for rejection in some patients and may work as part of a gene expression panel to diagnose rejection. These same PCR data were used to create PCR gene expression panels for diagnosis of acute rejection as discussed in example 17.

Non-parametric tests such as the Fisher Exact Test and Mann-Whitney U test are useful for choosing useful markers. They assess the ability of markers to discriminate between different classes as well as their significance. For example, one could use the median of all samples (including both non-rejector and rejector samples) as a threshold and apply the Fisher Exact test to the numbers of rejectors and non-rejectors above and below the threshold.

These methods were used to generate the data in Table 2D.

Example 14: Identification of diagnostic nucleotide sets for diagnosis of Cardiac Allograft Rejection using microarrays

Genes were identified which have expression patterns useful for the diagnosis and monitoring of acute cardiac allograft rejection. Further, sets of genes that work together in a diagnostic algorithm for allograft rejection were identified. Acute allograft rejection is a process that occurs in all solid organ transplantation including, heart, lung, liver, kidney, pancreas, pancreatic islet cell, intestine and others. Gene expression markers of acute cardiac rejection may be useful for diagnosis and monitoring of all

allograft recipients. Patients, patient clinical data and patient samples used in the discovery of markers below were derived from a clinical study described in example 5.

The collected clinical data was used to define patient or sample groups for correlation of expression data. Patient groups were identified for comparison. For example, a patient group that possesses a useful or interesting clinical distinction, verses a patient group that does not possess the distinction. Measures of cardiac allograft rejection were derived from the clinical data to divide patients (and patient samples) into groups with higher and lower rejection activity over some period of time or at any one point in time. Such data were rejection grades as determined from histological reading of the cardiac biopsy specimens by a pathologist and data measuring progression of end-organ damage, including depressed left ventricular dysfunction (decreased cardiac output, decreased ejection fraction, clinical signs of low cardiac output) and usage of inotropic agents (Kobashigawa 1998).

Mononuclear RNA samples were collected and prepared from patients who had recently undergone a cardiac allograft transplantation using the protocol described in example 2. The allograft rejection status at the time of sample collection was determined by examination of cardiac biopsies as described in example 5 and as summarized here.

300 patient samples were included in the analysis. Each patient sample was associated with a biopsy and other clinical data collected at the time of the sample. The cardiac biopsies were graded by a pathologist at the local center and by three centralized pathologists who read the biopsy slides from all four local centers in a blinded manner. Biopsy grades included 0, 1A, 1B, 2, 3A, and 3B. No grade 4 rejection was identified. Dependent variables were developed based on these grades using the local center pathology reading, the reading of a centralized and blinded pathologist, the highest of the readings, local or centralized and a consensus grade derived from all pathological readings. Samples were classified as no rejection or rejection in the following ways: Grade 0 vs. Grades 1-4, Grades 0 and 1A vs. Grades 1B-4, Grade 0 vs. Grade 3A, Grade 0 vs. Grades 1B-4, and Grade 0 vs. Grades 1B and 3A-4. Grade 0 samples were selected such that they were not immediately followed by an episode of acute rejection in the same patient. Comparing Grade 0 samples to Grade 3A samples gives the greatest difference between the rejection and no rejection groups on average.

Taking the highest of all pathologist readings has the effect of removing any sample from the no rejection class that was not a unanimous Grade 0. It also results in an increase in the number of rejection samples used in an analysis with the assumption that if a pathologist saw features of rejection, the call was likely correct and the other pathologists may have missed the finding. Many leading cardiac pathologists and clinicians believe that ISHLT grade 2 rejection does not represent significant acute rejection. Thus, for correlation analysis, exclusion of Grade 2 samples may be warranted. Clinical data were also used to determine criteria for including samples in the analysis. For example, a patient with an active infection or in the early post-transplant period (ongoing surgical inflammation) might have immune activation unrelated to rejection and thus be difficult to identify as patients without rejection. The strictest inclusion criteria required that samples be from patients who did not have a bacterial or viral infection, were at least two weeks post cardiac transplant, were asymptomatic and were not currently admitted to the hospital.

After preparation of RNA (example 2), amplification, labeling, hybridization, scanning, feature
extraction and data processing were done as described in Example 11, using the oligonucleotide
microarrays described in Example 9. The resulting log ratio of expression of Cy3 (patient sample)/
Cy5 (R50 reference RNA) was used for analysis.

Significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to discover genes
that were differentially expressed between the rejection and no-rejection groups. Many different
combinations of dependent variables, inclusion criteria, static/referenced, and data subsets were used in
SAM analysis to develop the primary lists of genes significantly differentially expressed between
rejection and no-rejection. As described in example 15, SAM assigns a false detection rate to each
gene identified as differentially expressed. The most significant of these genes were identified.

An exemplary analysis was the comparison of Grade 0 samples to Grade 3A-4 samples using SAM.
Data from the all the pathological readings was used to identify consensus Grade 0 samples and
samples with at least one reading of Grade 3A or above. Using this definition of rejection and no
rejection, expression profiles from rejection samples were compared to no rejection samples using
SAM. The analysis identified 7 genes with a FDR of 1%, 15 genes @ 1.4%, 35 genes @ 3.9%. Many
more genes were identified at higher FDR levels.

In Table 7, a number of SAM analyses are summarized. In each case the highest grade from the 3
pathologists was taken for analysis. No rejection and rejection classes are defined. Samples are either
used regardless of redundancy with respect to patients or a requirement is made that only one sample is
used per patient or per patient per class. The number of samples used in the analysis is given and the
lowest FDR achieved is noted.

Some of the genes identified by SAM as candidate rejection markers are noted in Table 2A and B.
SAM chooses genes as significantly different based on the magnitude of the difference between the
groups and the variation among the samples within each group. It is important to note that a gene
which is not identified by SAM as differentially expressed between rejection and no rejection may still
be a useful rejection marker because: 1. The microarray technology is not adequately sensitive to detect
all genes expressed at low levels. 2. A gene might be a useful member of a gene expression panel in
that it is a useful rejection marker only in a subset of patients. This gene may not be significantly
differentially expressed between all rejection and no rejection samples.

For the purposes of cross-validation of the results, the datasets were also divided into subsets to
compare analysis between two subsets of roughly half of the data. The types of subsets constructed
were as follows. First half/second half subsets were the first half of the samples and the second half of
the samples from a dataset ordered by sample number. Odd/even subsets used the same source, a
dataset ordered by sample number, but the odd subset consisted of every 2nd sample starting with the
first and the even subset consisted of every 2nd sample starting with the second sample, Center 14/other
subsets were the same datasets, divided by transplant hospital. The center 14 subset consisted of all
samples from patients at center 14, while the other subset consisted of all samples from the other three
centers (12,13, and 15). When a gene was found to be significantly differentially expressed in both sets
of data, a higher priority was put on that gene for development of a diagnostic test. This was reflected

in a "Array Score" value (Table 2B) that also considered the false detection rate for the gene and the importance of the gene in classification models (see example 17).

Alternatively one can divide samples into 10 equal parts and do 10-fold cross validation of the results of SAM.

Microarray data was also used to generate classification models for diagnosis of rejection as described in example 17. Genes identified through classification models as useful in the diagnosis of rejection are noted in in Table 2B in the column "models".

As genes were identified as useful rejection markers by microarray significance analysis, classification models, PCR analysis, or through searching the prior art, a variety of approaches were employed to discover genes that had similar expression behavior (coexpression) to the gene of interest. If a gene is a useful rejection marker, then a gene that is identified as having similar expression behavior is also likely to be a useful rejection marker. Hierarchical clustering (Eisen et al. 1998, see example 15) was used to identify co-expressed genes for established rejection markers. Genes were identified from the nearest branches of the clustering dendrogram. Gene expression profiles generated from 240 samples derived from transplant recipients were generated as described above. Hierarchical clustering was performed and co-expressed genes of rejection markers were identified. An example is shown in Figure 12. SEQ ID NO:85 was shown to be significantly differentially expressed between rejection and no rejection using both microarrays and PCR. Gene SEQ ID NO:3020 was identified by hierarchical clustering as closely co-expressed with SEQ ID NO:85. In table 2B, genes identified as co-expressed with established markers are identified as such by listing the SEQ ID that they are co-expressed with in the column labeled "clusters".

Some of the primers for real-time PCR validation were designed for each of the marker genes as described in Example 12 and are listed in Table 2C and the sequence listing. PCR expression measurements using these primers were used to validate array findings, more accurately measure differential gene expression and create PCR gene expression panels for diagnosis of rejection as described in example 17.

Alternative methods of analyzing the data may involve 1) using the sample channel without normalization by the reference channel, 2) using an intensity-dependent normalization based on the reference which provides a greater correction when the signal in the reference channel is large, 3) using the data without background subtraction or subtracting an empirically derived function of the background intensity rather than the background itself.

These methods were used to identify genes listed in Table 2B.

Example 15: Correlation and Classification Analysis

After generation and processing of expression data sets from microarrays as described in Example 11, a log ratio value is used for most subsequent analysis. This is the logarithm of the expression ratio for each gene between sample and universal reference. The processing algorithm assigns a number of flags to data that are of low signal to noise, saturated signal or are in some other way of low or uncertain quality. Correlation analysis can proceed with all the data (including the flagged data) or can be done on filtered data sets where the flagged data is removed from the set. Filtered data should have

less variability and noise and may result in more significant or predictive results. Flagged data contains all information available and may allow discovery of genes that are missed with the filtered data set. After filtering the data for quality as described above and in example 11, missing data are common in microarray data sets. Some algorithms don't require complete data sets and can thus tolerate missing values. Other algorithms are optimal with or require imputed values for missing data. Analysis of data sets with missing values can proceed by filtering all genes from the analysis that have more than 5%, 10%, 20%, 40%, 50%, 60% or other % of values missing across all samples in the analysis. Imputation of data for missing values can be done by a variety of methods such as using the row mean, the column mean, the nearest neighbor or some other calculated number. Except when noted, default settings for filtering and imputation were used to prepare the data for all analytical software packages.

In addition to expression data, clinical data are included in the analysis. Continuous variables, such as the ejection fraction of the heart measured by echocardiography or the white blood cell count can be used for correlation analysis. Any piece of clinical data collected on study subjects can be used in a correlation or classification analysis. In some cases, it may be desirable to take the logarithm of the values before analysis. These variables can be included in an analysis along with gene expression values, in which case they are treated as another "gene". Sets of markers can be discovered that work to diagnose a patient condition and these can include both genes and clinical parameters. Categorical variables such as male or female can also be used as variables for correlation analysis. For example, the sex of a patient may be an important splitter for a classification tree.

Clinical data are used as supervising vectors (dependent variables) for the significance or classification analysis of expression data. In this case, clinical data associated with the samples are used to divide samples in to clinically meaningful diagnostic categories for correlation or classification analysis. For example, pathologic specimens from kidney biopsies can be used to divide lupus patients into groups with and without kidney disease. A third or more categories can also be included (for example "unknown" or "not reported"). After generation of expression data and definition of supervising vectors, correlation, significance and classification analysis are used to determine which set of genes and set of genes are most appropriate for diagnosis and classification of patients and patient samples. Two main types of expression data analyses are commonly performed on the expression data with differing results and purposes. The first is significance analyses or analyses of difference. In this case, the goal of the analysis is to identify genes that are differentially expressed between sample groups and to assign a statistical confidence to those genes that are identified. These genes may be markers of the disease process in question and are further studied and developed as diagnostic tools for the indication. The second major type of analysis is classification analysis. While significance analysis identifies individual genes that are differentially expressed between sample groups, classification analysis identifies gene sets and an algorithm for their gene expression values that best distinguish sample (patient) groups. The resulting gene expression panel and algorithm can be used to create and implement a diagnostic test. The set of genes and the algorithm for their use as a diagnostic tool are often referred to herein as a "model". Individual markers can also be used to create a gene expression diagnostic model. However, multiple genes (or gene sets) are often more useful and accurate diagnostic tools.

Significance analysis for microarrays (SAM)

Significance analysis for microarrays (SAM) (Tusher 2001) is a method through which genes with a correlation between their expression values and the response vector are statistically discovered and assigned a statistical significance. The ratio of false significant to significant genes is the False Discovery Rate (FDR). This means that for each threshold there are some number of genes that are called significant, and the FDR gives a confidence level for this claim. If a gene is called differentially expressed between two classes by SAM, with a FDR of 5%, there is a 95% chance that the gene is actually differentially expressed between the classes. SAM will identify genes that are differentially expressed between the classes. The algorithm selects genes with low variance within a class and large variance between classes. The algorithm may not identify genes that are useful in classification, but are not differentially expressed in many of the samples. For example, a gene that is a useful marker for disease in women and not men, may not be a highly significant marker in a SAM analysis, but may be useful as part of a gene set for diagnosis of a multi-gene algorithm.

After generation of data from patient samples and definition of categories using clinical data as supervising vectors, SAM is used to detect genes that are likely to be differentially expressed between the groupings. Those genes with the highest significance can be validated by real-time PCR (Example 13) or can be used to build a classification algorithm as described here.

Classification

Classification algorithms are used to identify sets of genes and formulas for the expression levels of those genes that can be applied as diagnostic and disease monitoring tests. The same classification algorithms can be applied to all types of expression and proteomic data, including microarray and PCR based expression data. Examples of classification models are given in example 17. The discussion below describes the algorithms that were used and how they were used.

Classification and Regression Trees (CART) is a decision tree classification algorithm (Breiman 1984). From gene expression and or other data, CART can develop a decision tree for the classification of samples. Each node on the decision tree involves a query about the expression level of one or more genes or variables. Samples that are above the threshold go down one branch of the decision tree and samples that are not go down the other branch. Genes from expression data sets can be selected for classification building with CART by significant differential expression in SAM analysis (or other significance test), identification by supervised tree-harvesting analysis, high fold change between sample groups, or known relevance to classification of the target diseases. In addition, clinical data can be used as independent variables for CART that are of known importance to the clinical question or are found to be significant predictors by multivariate analysis or some other technique. CART identifies predictive variables and their associated decision rules for classification (diagnosis). CART also identifies surrogates for each splitter (genes that are the next best substitute for a useful gene in classification). Analysis is performed in CART by weighting misclassification costs to optimize desired performance of the assay. For example, it may be most important that the sensitivity of a test

for a given diagnosis be > 90%. CART models can be built and tested using 10 fold cross-validation or v-fold cross validation (see below). CART works best with a smaller number of variables (5-50). Multiple Additive Regression Trees (Friedman, JH 1999, MART) is similar to CART in that it is a classification algorithm that builds decision trees to distinguish groups. MART builds numerous trees for any classification problem and the resulting model involves a combination of the multiple trees. MART can select variables as it build models and thus can be used on large data sets, such as those derived from an 8000 gene microarray. Because MART uses a combination of many trees and does not take too much information from any one tree, it resists over training. MART identifies a set of genes and an algorithm for their use as a classifier.

A Nearest Shrunken Centroids Classifier can be applied to microarray or other data sets by the methods described by Tibshirani et al. 2002. This algorithms also identified gene sets for classification and determines their 10 fold cross validation error rates for each class of samples. The algorithm determines the error rates for models of any size, from one gene to all genes in the set. The error rates for either or both sample classes can are minimized when a particular number of genes are used. When this gene number is determined, the algorithm associated with the selected genes can be identified and employed as a classifier on prospective sample.

For each classification algorithm and for significance analysis, gene sets and diagnostic algorithms that are built are tested by cross validation and prospective validation. Validation of the algorithm by these means yields an estimate of the predictive value of the algorithm on the target population. There are many approaches, including a 10 fold cross validation analysis in which 10% of the training samples are left out of the analysis and the classification algorithm is built with the remaining 90%. The 10% are then used as a test set for the algorithm. The process is repeated 10 times with 10% of the samples being left out as a test set each time. Through this analysis, one can derive a cross validation error which helps estimate the robustness of the algorithm for use on prospective (test) samples. Any % of the samples can be left out for cross validation (v-fold cross validation, LOOCV). When a gene set is established for a diagnosis with an acceptable cross validation error, this set of genes is tested using samples that were not included in the initial analysis (test samples). These samples may be taken from archives generated during the clinical study. Alternatively, a new prospective clinical study can be initiated, where samples are obtained and the gene set is used to predict patient diagnoses.

Example 16: Acute allograft rejection: biopsy tissue gene expression profiling

Acute allograft rejection involves activation of recipient leukocytes and infiltration into the rejecting organ. For example, CD8 T-cells are activated by CD4 T-cells and enter the allograft where they destroy graft tissue. These activated, graft-associated leukocytes may reside in the graft, die or exit the graft. Upon exiting, the cells can find their way into the urine or blood (in the case of renal allografts), bile or blood (liver allografts) or blood (cardiac allografts). These activated cells have specific gene expression patterns that can be measured using microarrays, PCR or other methods. These gene expression patterns can be measured in the graft tissue (graft associated leukocytes), blood leukocytes, urine leukocytes or stool/biliary leukocytes. Thus graft associated leukocyte gene expression patterns are used to discover markers of activated leukocytes that can be measured outside the graft for diagnostic testing.

Renal biopsy and cardiac biopsy tissue specimens were obtained for gene expression profiling. The specimens were obtained at the time of allograft biopsy and were preserved by flash freezing in liquid nitrogen using standard approaches or immersion in an RNA stablization reagent as per the manufacturers recommendation (RNAlater, Qiagen, Valencia, CA). Biopsy allograft pathological evaluation was also obtained and samples were classified as having a particular ISHLT rejection grade (for cardiac) or acute rejection, chronic rejection, acute tubular necrosis or no disease (for renal).

28 renal biopsy tissue samples were transferred to RLT buffer, homogenized and RNA was prepared using RNeasy preparation kits (Qiagen, Valencia, CA). Average total RNA yield was 1.3 ug. Samples were subjected to on column DNAse digestion. 18 samples were derived from patients with ongoing acute allograft rejection and 10 were from controls with chronic rejection or acute renal failure.

RNA from the samples was used for amplification, labeling and hybridization to leukocyte arrays (example 11). Significance analysis for microarrays (SAM, Tusher 2001, Example 15) was used to identify genes that were differentially expressed between the acute rejection samples and controls. Leukocyte markers of acute rejection that are associated with the graft should be genes that are expressed at some level in activated leukocytes. Since leukocytes appear in graft tissue with some frequency with acute rejection, leukocyte genes associate with rejection are identified by SAM as upregulated in acute rejection in this experiment. 35 genes were identified as upregulated in acute rejection by SAM with less than a 5% false detection rate and 139 were detected with < 10.0% FDR. Results of this analysis are shown in Table 8.

For each of these genes, to 50mer oligonucleotide sequence was used to search NCBI databases including Unigene and OMIM. Genes were identified by sequence analysis to be either known leukocyte specific markers, known leukocyte expressed markers, known not to be leukocyte expressed or expression unknown. This information helped selected candidate leukocyte markers from all upregulated genes. This is necessary because some of the upregulated genes may have been expressed by renal tissue. Those genes that are leukocyte specific or leukocyte expressed were selected for evaluation by PCR in urine and blood samples from patients with and without acute allograft rejection (cardiac and renal). These genes are useful expression markers of acute rejection in allograft tissue specimens and may also be useful gene expression markers for the process in circulating leukocytes, or urine leukocytes. Genes with known leukocyte expression are noted in Table 8. In addition, some of the leukocyte expressed genes from this analysis were selected for PCR validation and development for diagnosis of acute cardiac rejection and are noted in Table 2.

Five cardiac rejection markers in the peripheral blood were assayed using real-time PCR in renal biopsy specimens. The average fold change for these genes between acute rejection (n = 6) and controls (n = 6) is given below. Work is ongoing to increase the number of samples tested and the significance of the results.

PCR assays of cardiac rejection peripheral blood markers in renal allograft tissue. R = rejection, NR = No rejection.

Gene	Fold change (R/NR)
Granzyme B	2.16
CD20	1.42
NK cell receptor	1.72
T-box 21	1.74
IL4	1.3

Markers of renal rejection that are secreted from cells may be measured in the urine or serum of patients as a diagnostic or screening assay for rejection. Genes with lower molecular weight are most likely to be filtered into the urine to be measured in this way. Standard immunoassays may be used to measure these proteins. In table 8, genes that are known to be secreted are noted.

Example 17: Microarray and PCR gene expression panels for diagnosis and monitoring of acute allograft rejection

Array panels / classification models

Using the methods of the invention, gene expression panels were discovered for screening and diagnosis of acute allograft rejection. Gene expression panels can be implemented for diagnostic testing using any one of a variety of technologies, including, but not limited to, microarrays and real-time PCR.

Using peripheral blood mononuclear cell RNA that was collected and prepared from cardiac allograft recipients as described in examples 2 and 5, leukocyte gene expression profiles were generated and analyzed using microarrays as described in examples 11, 13, and 15. 300 samples were analyzed. ISHLT rejection grades were used to divide patients into classes of rejection and no rejection. Multiple Additive Regression Trees (MART, Friedman, JH 1999, example 15) was used to build a gene expression panel and algorithm for the diagnosis of rejection with high sensitivity. Default settings for the implementaion of MART called TreeNet 1.0 (Salford Systems, San Diego, CA) were used except where noted.

82 Grade 0 (rejection) samples and 76 Grade 1B-4 (no rejection) samples were divided into training (80% of each class) and testing (20% of each class) sets. A MART algorithm was then developed on the training set to distinguish rejection from no rejection samples using a cost of 1.02:1 for misclassification of rejection as no rejection. The resulting algorithm was then used to classify the test samples. The algorithm correctly classified 51 of 66 (77%) no rejection samples in the training set and 9 of 16 (56%) no rejection samples in the test set. For rejection samples 64 of 64 (100%) were correctly classified in the training set and 12 of 12 were correctly classified in the test set. The algorithm used 37 genes. MART ranks genes by order of importance to the model. In order, the 37 genes were: SEQ IDs: 3058, 3030, 3034, 3069, 3081, 3072, 3041, 3052, 3048, 3045, 3059, 3075, 3024, 279, 3023, 3053, 3022, 3067, 3020, 3047, 3033, 3068, 3060, 3063, 3028, 3032, 3025, 3046, 3065, 3080, 3039, 3055, 49, 3080, 3038, 3071.

Another MART model was built by excluding samples derived from patients in the first month post transplant and from patients with known CMV infection. 20 Grade 0 (rejection) samples and 25 Grade 1B-4 (no rejection) samples were divided into training (80% of each class) and testing (20% of each class) sets. A MART algorithm was then developed on the training set to distinguish rejection from no rejection samples using default settings. The resulting algorithm was then used to classify the test samples. The algorithm correctly classified 100% of samples of both classes in the training and testing sets. However, this model required 169 genes. The sample analysis was done a second time with the only difference being requirement that all decision trees in the algorithm be composed of two nodes (single decision, "stump model"). In this case 15/16 no rejection samples were correctly identified in the training set and 4/4 no rejection samples were correctly identified in the test set. For the rejection samples, 17/19 were correctly identified in the training set and 5/6 were correctly classified in the test set. This model required 23 genes. In order of importance, they were: SEQ IDs: 3042, 2783, 3076, 3029, 3026, 2751, 3036, 3073, 3035, 3050, 3051, 3027, 3074, 3062, 3044, 3077, 2772, 3049, 3043, 3079, 3070, 3057, 3078.

Real-time PCR panels / classification models

PCR primers were developed for top rejection markers and used in real-time PCR assays on transplant patient samples as described in examples 12 and 13. This data was used to build PCR gene expression panels for diagnosis of rejection. Using MART (example 15) a 10-fold cross validated model was created to diagnose rejection using 12 no rejection samples (grade 0) and 10 rejection samples (grade 3A). Default settings were used with the exception of assigning a 1.02:1 cost for misclassification of rejection as no rejection and requirement that all decision trees be limited to 2 nodes ("stump model"). 20 genes were used in the model, including: SEQ IDs:101, 3021, 102, 2781, 78, 87, 86, 36, 77, 2766, 3018, 80, 3019, 2752, 79, 99, 3016, 2790, 3020, 3056, 88. The 10-fold cross-validated sensitivity for rejection was 100% and the specificity was 85%. Some PCR primers for the genes are listed in Table 2C and the sequence listing.

A different analysis of the PCR data was performed using the nearest shrunken centroids classifier (Tibshirani et al. 2002; PAM version 1.01, see example 15). A 10-fold cross validated model was created to diagnose rejection using 13 no rejection samples (grade 0) and 10 rejection samples (grade 3A). Default settings were used with the exception of using a prior probability setting of (0.5, 0.5). The algorithm derives algorithms using any number of the genes. A 3-gene model was highly accurate with a 10 fold cross-validated sensitivity for rejection of 90%, and a specificity of 85%.

The 3 genes used in this model were: SEQ IDs 2784, 79, and 2794. Some of the PCR primers used are given in Table 2C and the sequence listing. An ROC curve was plotted for the 3-gene model and is shown in Figure 13.

Example 18: Assay sample preparation

In order to show that XDx's leukocyte-specific markers can be detected in whole blood, we collected whole blood RNA using the PAXgene whole blood collection, stabilization, and RNA isolation kit (PreAnalytix). Varying amounts of the whole blood RNA were used in the initial RT reaction (1, 2, 4, and 8ug), and varying dilutions of the different RT reactions were tested (1:5, 1:10,

1:20, 1:40, 1:80, 1:160). We did real-time PCR assays with primers specific to XDx's markers and showed that we can reliably detect these markers in whole blood.

Total RNA was prepared from 14 mononuclear samples (CPT, BD) paired with 14 whole blood samples (PAXgene, PreAnalytix) from transplant recipients. cDNA was prepared from each sample using 2ug total RNA as starting material. Resulting cDNA was diluted 1:10 and Sybr green real-time PCR assays were performed.

For real-time PCR assays, Ct values of 15-30 are desired for each gene. If a gene's Ct value is much above 30, the result may be variable and non-linear. For PAX sample, target RNA will be more dilute than in CPT samples. cDNA dilutions must be appropriate to bring Ct values to less than 30. Ct values for the first 5 genes tested in this way are shown in the table below for both whole blood RNA (PAX) and mononuclear RNA (CPT).

Gene	Ct PAX	Ct CPT
CD20	27.41512	26.70474
4761	28.45656	26.52635
3096	29.09821	27.83281
GranzymeB	31.18779	30.56954
IL4	33.11774	34.8002
Actin	19.17622	18.32966
B-GUS	26.89142	26.92735

With one exception, the genes have higher Ct values in whole blood. Using this protocol, all genes can be detected with Cts <35. For genes found to have Ct values above 30 in target samples, less diluted cDNA may be needed.

Example 19: Allograft rejection diagnostic gene sequence analysis

Gene products that are secreted from cells or expressed as surface proteins have special diagnostic utility in that an assay may be developed to detect relative quantities of proteins in blood plasma or serum. Secreted proteins may also be detectable in urine, which may be a useful sample for the detection of rejection in renal allograft recipients. Cell surface markers may be detected using antigen specific antibodies in ELISA assays or using flow srting techniques such as FACS.

Each gene that is found to be differentially regulated in one population of patients has several potential applications. It may be a target for new pharmaceuticals, a diagnostic marker for a condition, a benchmark for titrating drug delivery and clearance, or used in screening small molecules for new therapeutics. Any of these applications may be improved by an understanding of the physiologic function and localization of the gene product in vivo and by relating those functions to known diseases and disorders. Identifying the basic function of each candidate gene helps identify the signaling or metabolic pathways the gene is a part of, leading us to investigate other members of those pathways as potential diagnostic markers or targets of interest to drug developers.

For each of the markers in table 2, we attempted to identify the basic function and subcellular localization of the gene. These results are summarized in Table 9. In addition to initial DNA sequencing and processing, sequence analysis, and analysis of novel clones, information was obtained from the following public resources: Online Mendelian Inheritance in Man at the NCBI, LocusLink at the NCBI, the SWISS-PROT database, and Protein Reviews on the Web. For each marker represented by a curated reference mRNA from the RefSeq project, the corresponding reference protein accession number is listed. Curated sequences are those that have been manually processed by NCBI staff to represent the best estimate of the mRNA sequence as it is transcribed, based on alignments of draft DNA sequence, predicted initiation, termination and splice sites, and submissions of EST and full-length mRNA sequences from the scientific community.

These methods were used to derive the data in Table 2E.

Example 20: Detection of proteins expressed by diagnostic gene sequences

One of ordinary skill in the art is aware of many possible methods of protein detection. The following example illustrates one possible method.

The designated coding region of the sequence is amplified by PCR with adapter sequences at either end for subcloning. An epitope or other affinity "tag" such as a "His-tag" may be added to facilitate purification and/or detection of the protein. The amplified sequence is inserted into an appropriate expression vector, most typically a shuttle vector which can replicate in either bacteria, most typically E. coli, and the organism/cell of choice for expression such as a yeast or mammalian cell. Such shuttle vectors typically contain origins of replication for bacteria and an antibiotic resistance marker for selection in bacteria, as well as the relevant replication and selection sequences for transformation/transfection into the ultimate expression cell type. In addition, the sequence of interest is inserted into the vector so that the signals necessary for transcription (a promoter) and translation operably linked to the coding region. Said expression could be accomplished in bacteria, fungi, or mammalian cells, or by in vitro translation.

The expression vector would then typically be used to transform bacteria and clones analyzed to ensure that the proper sequence had been inserted into the expression vector in the productive orientation for expression. Said verified expression vector is then transfected into a host cell and transformants selected by a variety of methods including antibiotic resistance or nutritional complementation of an auxotrophic marker. Said transformed cells are then grown under conditions conducive to expression of the protein of interest, the cells and conditioned media harvested, and the protein of interest isolated from the most enriched source, either the cell pellet or media.

The protein is then be isolated by standard of chromatographic or other methods, including immunoaffinity chromatography using the affinity "tag" sequence or other methods, including cell fractionation, ion exchange, size exclusion chromatography, or selective precipitation. The isolated and purified protein is then be used as an antigen to generate specific antibodies. This is accomplished by standard methods including injection into heterologous species with an adjuvant, isolation of monoclonal antibodies from mice, or in vitro selection of antibodies from bacteriophage display antibody libraries. These antibodies are then used to detect the presence of the indicated protein of interest in a complex bodily fluid using standard methods such as ELISA or RIA.

Example 21: Detecting changes in the rate of hematopoiesis

Gene expression profiling of blood cells from cardiac allograft recipients was done using microarrays and real-time PCR as described in other examples herein.

Two of the genes in that were most correlated with cardiac transplant acute rejection with both microarrays and PCR were hemoglobin Beta and 2,3 DPGM. These genes are well know to be specific markers of erythrocyte lineages. This correlation was found using both purified peripheral mononuclear cells and whole blood RNA preparations.

Analysis of the five genes from the PCR data most strongly correlated with rejection showed that their expression levels were extremely highly correlated within each other (R2 > 0.85).

Gene	Hs	Acc	SEQ ID No
hemoglobin, beta (HBB)	Hs.155376	NM_000518	86
2,3-bisphosphoglycerate mutase (BP(	Hs.198365	X04327	87
cDNA FLJ20347	Hs.102669	AK000354	94
602620663F1cDNA	Hs.34549	AI123826	107
HA1247 cDNA	Hs.33757	AI114652	91

This suggested that they were all elevated as part of a single response or process. When the microarray data was used to cluster these genes with each other and the other genes on the microarray, we found that these five genes clustered reasonably near each and of the other array genes which clustered tightly with them, four of the top 40 or so were platelet related genes. In addition, these a number of these genes clustered closely with CD34. CD34 is a marker of hematopoietic stem cells and is seen in the peripheral blood with increased hematopoisis.

CD34, platelet RNA and erythrocyte RNA all mark immature or progenitor blood cells and it is clear that theses marker of acute rejection are part of a coordinated hematopoietic response. A small increase in the rate of production of RBCs and platelets may result in large fold changes in RNA levels. Immune activation from acute rejection may lead to increased hamatopoiesis in the bone marrow and non-marrow sites. This leads to an increase in many lineages because of the lack of complete specificity of the marrow response. Alternatively, increased hematopoiesis may occur in a transplant recipient due to an infection (viral or other), allergy or other stimulus to the system. This results in production of cells or a critical mass of immune cells that can cause rejection. In this scenario, monitoring for markers of immune activation would provide an opportunity for early diagnosis.

Table 1

Disease Classification	Disease/Patient Group
Cardiovascular Disease	Atherosclerosis Unstable angina Myocardial Infarction Restenosis after angioplasty Congestive Heart Failure Myocarditis Endocarditis Endothelial Dysfunction Cardiomyopathy Cardiovascular drug use
Infectious Disease	Hepatitis A, B, C, D, E, G Malaria Tuberculosis HIV Pneumocystis Carinii Giardia Toxoplasmosis Lyme Disease Rocky Mountain Spotted Fever Cytomegalovirus Epstein Barr Virus Herpes Simplex Virus Clostridium Dificile Colitis Meningitis (all organisms) Pneumonia (all organisms) Urinary Tract Infection (all organisms) Infectious Diarrhea (all organisms) Anti-infectious drug use
Angiogenesis	Pathologic angiogenesis Physiologic angiogenesis Treatment induced angiogenesis Pro or anti-angiogenic drug use
Transplant Rejection	Heart Lung Liver Pancreas Bowel Bone Marrow Stem Cell Graft versus host disease Transplant vasculopathy Skin Cornea Islet Cells Kidney Xenotransplants Mechanical Organ Immunosupressive drug use
Hematological Disorders	Anemia – Iron Deficiency Anemia – B12, Folate deficiency Anemia – Aplastic Anemia – hemolytic Anemia – Renal failure Anemia – Chronic disease Polycythemia rubra vera Pernicious anemia Idiophic Thrrombocytopenic purpura Thrombotic Thrombocytopenic purpura Essential thrombocytosis Leukemia Cytopenias due to immunosupression Cytopenias due to Chemotherapy Myelodysplasia

Table 2A.

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
HSRRN18S	18S ribosomal RNA	1	NA	X03205	333
ACTB	Actin, beta	2	Hs.288061	NM_001101	334
GUSB	Glucuronidase, beta	3	Hs.183868	NM_000181	335
B2M	beta 2 microglobulin	4	Hs.75415	NM_004048	336
TSN	Translin	5	Hs.75066	NM_004622	337
CCR7	1707	6	Hs.1652	NM_001838	338
IL1R2	4685-IL1R	7	Hs.25333	NM_004633	339
AIF-1	Allograft inflammatory factor 1, all variants	8	Hs.76364	NM_004847	340
ALAS2	ALAS2	9	Hs.323383	NM_000032.1	341
APELIN	APELIN	10	Hs.303084	NM_017413	342
CD80	B7-1, CD80	11	Hs.838	NM_005191	343
EPB41	Band 4.1	12	Hs.37427	NM_004437	344
CBLB	c-cbl-B	13	Hs.3144	NM_004351	345
CCR5	CCR5	14	Hs.54443	NM_000579	346
MME	CD10	15	Hs.1298	NM_000902	347
KLRC1	CD159a	16	Hs.74082	NM_002259	348
FCGR3A	CD16	17	Hs.176663	NM_000569	349
FCGR3B	CD16b	18	Hs.372679	NM_000570	350
LAG3	CD223	19	Hs.74011	NM_002286	351
PECAM1	CD31	20	Hs.78146	NM_000442	352
CD34	CD34	21	Hs.374990	NM_001773	353
FCGR1A	CD64	22	Hs.77424	NM_000566	354
TFRC	CD71 = T9, transferrin receptor	23	Hs.77356	NM_003234	355
CMA1	chymase	24	Hs.135626	NM_001836	356
KIT	c-Kit	25	Hs.81665	NM_000222	357
MPL	c-mpl	26	Hs.84171	NM_005373	358
EphB6	EphB6	27	Hs.3796	NM_004445	359
EPOR	EPO-R	28	Hs.127826	NM_000121.2	360
Foxp3	Foxp3	29	Hs.247700	NM_014009	361
GATA1	GATA1	30	Hs.765	NM_002049	362
ITGA2B	GP IIb	31	NM_000419.2	NM_000419	363
GNLY	granulysin	32	Hs.105806	NM_006433	364
GZMA	GZMA	33	Hs.90708	NM_006144	365
HBA	hemoglobin, alpha 1	34	Hs.398636	NM_000558.3	366
HBZ	hemoglobin, zeta	35	Hs.272003	NM_005332.2	367
HBB	hemoglobin, beta	36	Hs.155376	NM_000518.4	368
HBD	hemoglobin, delta	37	Hs.36977	NM_000519.2	369
HBE	hemoglobin, epsilon 1	38	Hs.117848	NM_005330	370
HBG	hemoglobin, gamma A	39	Hs.283108	NM_000559.2	371
HBQ	hemoglobin, theta 1	40	Hs.247921	NM_005331	372
HLA-DP	MH/c, class II, DP alpha 1	41	Hs.198253	NM_033554	373
HLA-DQ	MHC, class II, DQ alpha 1	42	Hs.198253	NM_002122	374
HLA-DRB	MHC, class II, DR beta 1	43	Hs.375570	NM_002124.1	375
ICOS	ICOS	44	Hs.56247	NM_012092	376
IL18	IL18	45	Hs.83077	NM_001562	377
IL3	interleukin 3 (colony-stimulating factor, multiple)	46	Hs.694	NM_000588	378
ITGA4	Integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	47	Hs.40034	NM_000885	379

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
ITGAM	integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide)	48	Hs.172631	NM_000632	380
ITGB7	integrin, beta 7	49	Hs.1741	NM_000889	381
CEBPB	LAP, CCAAT/enhancer binding protein (C/EBP), beta	50	Hs.99029	NM_005194	382
NF-E2	NF-E2	51	Hs.75643	NM_006163	383
PDCD1	programmed cell death 1, PD-1	52	Hs.158297	NM_005018	384
PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	53	Hs.81564	NM_002619	385
PRKCQ	protein kinase C, theta	54	Hs.211593	NM_006257.1	386
PPARGC1	PPARgamma	55	Hs.198468	NM_013261	387
RAG1	recombination activating gene 1	56	Hs.73958	NM_000448	388
RAG2	recombination activating gene 2	57	Na	NM_000536	389
CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1) (SDF-1)	58	Hs.237356	NM_000609	390
TNFRSF4	tumor necrosis factor receptor superfamily, member 4	59	Hs.129780	NM_003327	391
TNFSF4	tumor necrosis factor (ligand) superfamily, member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa)	60	Hs.181097	NM_003326	392
TPS1	tryptase, alpha	61	Hs.334455	NM_003293	393
ADA	ADA adenosine deaminase	62	Hs.1217	NM_000022	394
CPM	Carboxypeptidase M	63	Hs.334873	NM_001874.1	395
CSF2	colony stimulating factor, GM-CSF	64	Hs.1349	NM_000758.2	396
CSF3	colony stimulating factor 3, G-CSF	65	Hs.2233	NM_172219	397
CRP	C-reactive protein, pentraxin-related (CRP),	66	Hs.76452	NM_000567.1	398
FLT3	FMS-Related Tyrosine Kinase 3	67	Hs.385	NM_004119	399
GATA3	GATA binding protein 3	68	Hs.169946	NM_002051.1	400
IL7R	Interleukin 7 receptor	69	Hs.362807	NM_002185.1	401
KLF1	Kruppel-like factor 1 (erythroid), EKLF	70	Hs.37860	NM_006563.1	402
LCK	lymphocyte-specific protein tyrosine kinase	71	Hs.1765	NM_005356.2	403
LEF1	lymphoid enhancer-binding factor 1	72	Hs.44865	NM_016269.2	404
PLAUR	Urokinase-type Plasminogen Activator Receptor, CD87, uPAR	73	Hs.179657	NM_002659.1	405
TNFSF13B	Tumor necrosis factor (ligand) superfamily, member 13b, BlyS/TALL-1/BAFF	74	Hs.270737	NM_006573.3	406
IL8	Interleukin 8	75	Hs.624	NM_000584	407
GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	76	Hs.1051	NM_004131	408
TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	77	Hs.2007	NM_000639	409

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	78	Hs.46465	NM_006019	410
PRF1	Perforin 1 (pore forming protein)	79	Hs.2200	NM_005041	411
IL4	Interleukin 4	80	Hs.73917	NM_000589	412
IL13	Interleukin 13	81	Hs.845	NM_002188	413
CTLA4	Cytotoxic T-lymphocyte-associated protein 4	82	Hs.247824	NM_005214	414
CD8A	CD8 antigen, alpha polypeptide (p32)	83	Hs.85258	NM_001768	415
BY55	Natural killer cell receptor, immunoglobulin superfamily member	84	Hs.81743	NM_007053	416
OID_4460	EST	85	Hs.205159	AF150295	417
HBB	Hemoglobin, beta	86	Hs.155376	NM_000518	418
BPGM	2,3-bisphosphoglycerate mutase	87	Hs.198365	NM_001724	419
MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	88	Hs.154672	NM_006636	420
TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	89	Hs.352018	NM_000593	421
KPNA6	Karyopherin alpha 6 (importin alpha 7)	90	Hs.301553	AW021037	422
OID_4365	Mitochondrial solute carrier	91	Hs.300496	AI114652	423
IGHM	Immunoglobulin heavy constant mu	92	Hs.300697	BC032249	424
OID_573	KIAA1486 protein	93	Hs.210958	AB040919	425
OID_873	KIAA1892 protein	94	Hs.102669	AK000354	426
OID_3	EST	95	Hs.104157	AW968823	427
CXCR4	Chemokine (C-X-C motif) receptor 4	96	Hs.89414	NM_003467	428
CD69	CD69 antigen (p60, early T-cell activation antigen)	97	Hs.82401	NM_001781	429
CCL5	Chemokine (C-C motif) ligand 5 (RANTES, SCYA5)	98	Hs.241392	NM_002985	430
IL6	Interleukin 6	99	Hs.93913	NM_000600	431
IL2	Interleukin 2	100	Hs.89679	NM_000586	432
KLRF1	Killer cell lectin-like receptor subfamily F, member 1	101	Hs.183125	NM_016523	433
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	102	Hs.80887	NM_002350	434
IL2RA	Interleukin 2 receptor, alpha	103	Hs.1724	NM_000417	435
CCL4	Chemokine (C-C motif) ligand 4, SCYA4	104	Hs.75703	NM_002984	436
OID_6207	EST	105	Hs.92440	D20522	437
ChGn	Chondroitin beta 1,4 N-acetylgalactosaminyltransferase	106	Hs.11260	NM_018371	438
OID_4281	EST	107	Hs.34549	AA053887	439
CXCL9	Chemokine (C-X-C motif) ligand 9 (MIG)	108	Hs.77367	NM_002416	440
CXCL10	Chemokine (C-X-C motif) ligand 10, SCYB10	109	Hs.2248	NM_001565	441

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
IL17	Interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 8)	110	Hs.41724	NM_002190	442
IL15	Interleukin 15	111	Hs.168132	NM_000585	443
IL10	Interleukin 10	112	Hs.193717	NM_000572	444
IFNG	Interferon, gamma	113	Hs.856	NM_000619	445
HLA-DRB1	Major histocompatibility complex, class II, DR beta 1	114	Hs.308026	NM_002124	446
CD8B1	CD8 antigen, beta polypeptide 1 (p37)	115	Hs.2299	NM_004931	447
CD4	CD4 antigen (p55)	116	Hs.17483	NM_000616	448
CXCR3	Chemokine (C-X-C motif) receptor 3, GPR9	117	Hs.198252	NM_001504	449
OID_7094	XDx EST 479G12	118	NA	NA	450
OID_7605	EST	119	Hs.109302	AA808018	451
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	120	Hs.789	NM_001511	452
OID_253	EST	121	Hs.83086	AK091125	453
GPI	Glucose phosphate isomerase	122	Hs.409162	NM_000175	454
CD47	CD47 antigen (Rh-related antigen, integrin-associated signal transducer)	123	Hs.82685	NM_001777	455
HLA-F	Major histocompatibility complex, class I, F	124	Hs.377850	NM_018950	456
OID_5350	EST	125	Hs.4283	AK055687	457
TCRGC2	T cell receptor gamma constant 2	126	Hs.112259	M17323	458
OID_7016	EST	127	NA	BI018696	459
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	128	Hs.196384	NM_000963	460
OID_5847	Hypothetical protein FLJ32919	129	Hs.293224	NM_144588	461
PRDM1	PR domain containing 1, with ZNF domain	130	Hs.388346	NM_001198	462
CKB	Creatine kinase, Brain	131	Hs.173724	NM_001823	463
TNNI3	Troponin I, cardiac	132	Hs.351382	NM_000363	464
TNNT2	Troponin T2, cardiac	133	Hs.296865	NM_000364	465
MB	Myoglobin	134	Hs.118836	NM_005368	466
SLC7A11	Solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	135	Hs.6682	NM_014331	467
TNFRSF5	tumor necrosis factor receptor superfamily, member 5; CD40	136	Hs.25648	NM_001250	468
TNFRSF7	tumor necrosis factor receptor superfamily, member 7; CD27	137	Hs.355307	NM_001242	469
CD86	CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)	138	Hs.27954	NM_175862	470
AIF1v2	Allograft inflammatory factor 1, splice variant 2	139	Hs.76364	NM_004847	471
EBV BCLF-1	BCLF-1 major capsid	140	NA	AJ507799	472
EBV EBV	EBNA repetitive sequence	141	NA	AJ507799	473
CMV p67	pp67	142	NA	X17403	474
CMV TRL7	c6843-6595	143	NA	X17403	475
CMV IE1e3	IE1 exon 3	144	NA	X17403	476

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
CMV IE1e4	IE1 exon 4 (40 variants)	145	NA	X17403	477
EBV EBNA-1	EBNA-1 coding region	146	NA	AJ507799	478
EBV BZLF-1	Zebra gene	147	NA	AJ507799	479
EBV EBN	EBNA repetitive sequence	148	NA	AJ507799	480
EBV EBNA-LP	Short EBNA leader peptide exon	149	NA	AJ507799	481
CMV IE1	IE1S	150	NA	X17403	482
CMV IE1	IE1-MC (exon 3)	151	NA	X17403	483
CLC	Charot-Leyden crystal protein	152	Hs.889	NM_001828	484
TERF2IP	telomeric repeat binding factor 2, interacting protein	153	Hs.274428	NM_018975	485
HLA-A	Major histocompatibility complex, class I, A	154	Hs.181244	NM_002116	486
OID_5891	EST 3' end	155	None	AW297949	487
MSCP	mitochondrial solute carrier protein	156	Hs.283716	NM_018579	488
DUSP5	dual specificity phosphatase 5	157	Hs.2128	NM_004419	489
PRO1853	Hypothetical protein PRO1853	158	Hs.433466	NM_018607	490
OID_6420	73A7, FLJ00290 protein	159	Hs.98531	AK090404	491
CDSN	Corneodesmosin	160	Hs.507	NM_001264	492
OID_4269	EST	161	Hs.44628	BM727677	493
RPS25	Ribosomal protein S25	162	Hs.409158	NM_001028	494
GAPD	Glyceraldehyde-3-phosphate dehydrogenase	163	Hs.169476	NM_002046	495
RPLP1	Ribosomal protein, large, P1	164	Hs.424299	NM_001003	496
OID_5115	qz23b07.x1 cDNA, 3' end /clone=IMAGE:2027701	165	NA	AI364926	497
SLC9A8	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 8	166	Hs.380978	AB023156	498
OID_1512	IMAGE:3865861 5_clone 5'	167	Hs.381302	BE618004	499
POLR2D	Polymerase (RNA) II (DNA directed) polypeptide D	168	Hs.194638	NM_004805	500
ARPC3	Actin related protein 2/3 complex, subunit 3, 21kDa	169	Hs.293750	NM_005719	501
OID_6282	EST 3' end	170	Hs.17132	BC041913	502
PRO1073	PRO1073 protein	171	Hs.356442	AF001542	503
OID_7222	EST, weakly similar to A43932 mucin 2 precursor, intestinal	172	Hs.28310	BG260891	504
FPRL1	Formyl peptide receptor-like 1	173	Hs.99855	NM_001462	505
FKBPL	FK506 binding protein like	174	Hs.99134	NM_022110	506
PREB	Prolactin regulatory element binding	175	Hs.279784	NM_013388	507
OID_1551	Hypothetical protein LOC200227	176	Hs.250824	BE887646	508
OID_7595	DKFZP566F0546 protein	177	Hs.144505	NM_015653	509
RNF19	Ring finger protein 19	178	Hs.48320	NM_015435	510
SMCY	SMC (mouse) homolog, Y chromosome (SMCY)	179	Hs.80358	NM_004653	511
OID_4184	CMV HCMVUL109	180	NA	X17403	512
OID_7504	Hypothetical protein FLJ35207	181	Hs.86543	NM_152312	513
DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	182	Hs.9683	NM_006260	514
ARHU	Ras homolog gene family, member U	183	Hs.20252	NM_021205	515
OID_7200	Hypothetical protein FLJ22059	184	Hs.13323	NM_022752	516

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
SERPINB2	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2	185	Hs.75716	NM_002575	517
ENO1	Enolase 1, alpha	186	Hs.254105	NM_001428	518
OID_7696	EST 3' end	187	Hs.438092	AW297325	519
OID_4173	CMV HCMVTRL2 (IRL2)	188	NA	X17403	520
CSF2RB	Upstream variant mRNA of colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	189	Hs.285401	AL540399	521
OID_7410	CM2-LT0042-281299-062-e11 LT0042 cDNA, mRNA sequence	190	Hs.375145	AW837717	522
OID_4180	CMV HCMVUS28	191	NA	X17403	523
OID_5101	EST	192	Hs.144814	BG461987	524
MOP3	MOP-3	193	Hs.380419	NM_018183	525
RPL18A	Ribosomal protein L18a	194	Hs.337766	NM_000980	526
INPP5A	Inositol polyphosphate-5-phosphatase, 40kDa	195	Hs.124029	NM_005539	527
hIAN7	Immune associated nucleotide	196	Hs.124675	BG772661	528
RPS29	Ribosomal protein S29	197	Hs.539	NM_001032	529
OID_6008	EST 3' end	198	Hs.352323	AW592876	530
OID_4186	CMV HCMVUL122	199	NA	X17403	531
VNN2	vanin 2	200	Hs.121102	NM_004665	532
OID_7703	KIAA0907 protein	201	Hs.24656	NM_014949	533
OID_7057	480F8	202	NA	480F8	534
OID_4291	EST	203	Hs.355841	BC038439	535
OID_1366	EST	204	Hs.165695	AW850041	536
EEF1A1	Eukaryotic translation elongation factor 1 alpha 1	205	Hs.422118	NM_001402	537
PA2G4	Proliferation-associated 2G4, 38kDa	206	Hs.374491	NM_006191	538
GAPD	Glyceraldehyde-3-phosphate dehydrogenase	207	Hs.169476	NM_002046	539
CHD4	Chromodomain helicase DNA binding protein 4	208	Hs.74441	NM_001273	540
OID_7951	E2F-like protein (LOC51270)	209	Hs.142908	NM_016521	541
DAB1	Disabled homolog 1 (Drosophila)	210	Hs.344127	NM_021080	542
OID_3406	Hypothetical protein FLJ20356	211	Hs.61053	NM_018986	543
OID_6986	462H9_EST	212	Hs.434526	AK093608	544
OID_5962	EST 3' end	213	Hs.372917	AW452467	545
OID_5152	EST 3' end	214	Hs.368921	AI392805	546
S100A8	S100 calcium-binding protein A8 (calgranulin A)	215	Hs.416073	NM_002964	547
HNRPU	HNRPU Heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)	216	Hs.103804	BM467823	548
ERCC5	Excision repair cross-complementing rodent repair deficiency, complementation group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome))	217	Hs.48576	NM_000123	549
RPS27	Ribosomal protein S27 (metallopanstimulin 1)	218	Hs.195453	NM_001030	550
ACRC	acidic repeat containing (ACRC),	219	Hs.135167	NM_052957	551

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PSMD11	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	220	Hs.90744	AI684022	552
OID_1016	FLJ00048 protein	221	Hs.289034	AK024456	553
OID_1309	AV706481 cDNA	222	None	AV706481	554
OID_7582	Weakly similar to ZINC FINGER PROTEIN 142	223	Hs.16493	AK027866	555
OID_4317	ta73c09.x1 3' end /clone=IMAGE:2049712 Ribosomal Protein S15	224	Hs.387179	AI318342	556
OID_5889	3' end /clone=IMAGE:3083913	225	Hs.255698	AW297843	557
UBL1	Ubiquitin-like 1 (sentrin)	226	Hs.81424	NM_003352	558
OID_3687	EST	227	None	W03955	559
OID_7371	EST 5'	228	Hs.290874	BE730505	560
SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	229	Hs.109051	NM_031286	561
SEMA7A	Sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	230	Hs.24640	NM_003612	562
OID_5708	EST 3' end	231	Hs.246494	AW081540	563
OID_5992	EST 3' end	232	Hs.257709	AW467992	564
IL21	Interleukin 21	233	Hs.302014	NM_021803	565
HERC3	Hect domain and RLD 3 (HERC3)	234	Hs.35804	NM_014606	566
OID_7799	AluJo/FLAM SINE/Alu	235		AW837717	567
P11	26 serine protease	236	Hs.997	NM_006025	568
OID_7766	EST 3' end	237	Hs.437931	AW294711	569
TIMM10	translocase of inner mitochondrial membrane 10 (yeast) homolog (TIMM10)	238	Hs.235750	NM_012456	570
EGLN1	Egl nine homolog 1 (C. elegans)	239	Hs.6523	AJ310543	571
TBCC	Tubulin-specific chaperone c	240	Hs.75064	NM_003192	572
RNF3	Ring finger protein 3	241	Hs.8834	NM_006315	573
OID_6451	170F9, hypothetical protein FLJ21439	242	Hs.288872	AL834168	574
CCNDBP1	cyclin D-type binding-protein 1 (CCNDBP1)	243	Hs.36794	NM_012142	575
OID_8063	MUC18 gene exons 1&2	244	NA	X68264	576
SUV39H1	Suppressor of variegation 3-9 homolog 1 (Drosophila)	245	Hs.37936	NM_003173	577
HSPC048	HSPC048 protein	246	Hs.278944	NM_014148	578
OID_5625	EST 3' end from T cells	247	Hs.279121	AW063780	579
WARS	Tryptophanyl-tRNA synthetase	248	Hs.82030	NM_004184	580
OID_6823	107H8	249	Hs.169610	AL832642	581
OID_7073	119F12	250	Hs.13264	AL705961	582
OID_5339	EST 3' end	251	Hs.436022	AI625119	583
OID_4263	fetal retina 937202 cDNA clone IMAGE:565899	252	Hs.70877	AA136584	584
MGC26766	Hypothetical protein MGC26766	253	Hs.288156	AK025472	585
SERPINB11	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 11	254	Hs.350958	NM_080475	586
OID_6711	58G4, IMAGE:4359351 5'	255	none	BF968628	587
RNF10	Ring finger protein 10	256	Hs.5094	NM_014868	588
MKRN1	Makorin, ring finger protein, 1	257	Hs.7838	NM_013446	589
RPS16	ribosomal protein S16	258	Hs.397609	NM_001020	590

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
BAZ1A	Bromodomain adjacent to zinc finger domain, 1A	259	Hs.8858	NM_013448	591
OID_5998	EST 3' end	260	Hs.330268	AW468459	592
ATP5L	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g	261	Hs.107476	NM_006476	593
OID_6393	52B9	262	NA	52B9	594
RoXaN	Ubiquitous tetratricopeptide containing protein RoXaN	263	Hs.25347	BC004857	595
NCBP2	Nuclear cap binding protein subunit 2, 20kDa	264	Hs.240770	NM_007362	596
OID_6273	EST 3' end	265	Hs.158976	AW294774	597
HZF12	zinc finger protein 12	266	Hs.164284	NM_033204	598
CCL3	Chemokine (C-C motif) ligand 3	267	Hs.73817	D90144	599
OID_4323	IMAGE:1283731 3'	268	Hs.370770	AA744774	600
OID_5181	tg93h12.x1 NCI_CGAP_CLL1 cDNA clone IMAGE:2116391 3' similar to contains TAR1.t1 MER22	269	NA	AI400725	601
PRDX4	Peroxiredoxin 4	270	Hs.83383	NM_006406	602
BTK	Bruton agammaglobulinemia tyrosine kinase	271	Hs.159494	NM_000061	603
OID_6298	Importin beta subunit mRNA	272	Hs.180446	AI948513	604
PGK1	Phosphoglycerate kinase 1	273	Hs.78771	NM_000291	605
TNFRSF10A	Tumor necrosis factor receptor superfamily, member 10a	274	Hs.249190	NM_003844	606
ADM	adrenomedullin	275	Hs.394	NM_001124	607
OID_357	138G5	276	NA	138G5	608
C20orf6	461A4 chromosome 20 open reading frame 6	277	Hs.88820	NM_016649	609
OID_3226	DKFZP564O0823 protein	278	Hs.105460	NM_015393	610
ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	279	Hs.75811	NM_004315	611
ATF5	Activating transcription factor 5	280	Hs.9754	NM_012068	612
OID_4887	hypothetical protein MGC14376	281	Hs.417157	NM_032895	613
OID_4239	EST	282	Hs.177376	BQ022840	614
MDM2	Mouse double minute 2, homolog of; p53-binding protein (MDM2), transcript variant MDM2,	283	Hs.170027	NM_002392	615
XRN2	5'-3' exoribonuclease 2	284	Hs.268555	AF064257	616
OID_6039	Endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4 (EDG4)	285	Hs.122575	BE502246	617
OID_4210	IMAGE:4540096	286	Hs.374836	AI300700	618
OID_7698	EST 3' end	287	Hs.118899	AA243283	619
PRKRA	Protein kinase, interferon-inducible double stranded RNA dependent activator	288	Hs.18571	NM_003690	620
OID_4288	IMAGE:2091815	289	Hs.309108	AI378046	621
OID_5620	EST 3' end from T cells	290	Hs.279116	AW063678	622
OID_7384	EST 5'	291	Hs.445429	BF475239	623
OID_1209	EST Weakly similar to hypothetical protein FLJ20378	292	Hs.439346	C14379	624
CDKN1B	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)	293	Hs.238990	NM_004064	625

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PLOD	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)	294	Hs.75093	NM_000302	626
OID_5128	EST	295	Hs.283438	AK097845	627
OID_5877	EST 3' end	296	Hs.438118	AW297664	628
FZD4	Frizzled (Drosophila) homolog 4	297	Hs.19545	NM_012193	629
HLA-B	Major histocompatibility complex, class I, B	298	Hs.77961	NM_005514	630
OID_5624	EST 3' end from T cells	299	Hs.279120	AW063921	631
FPR1	Formyl peptide receptor 1	300	Hs.753	NM_002029	632
ODF2	Outer dense fiber of sperm tails 2	301	Hs.129055	NM_153437	633
OID_5150	tg04g01.x1 cDNA, 3' end /clone=IMAGE:2107824	302	Hs.160981	AI392793	634
OID_5639	EST 3' end from T cells	303	Hs.279139	AW064243	635
OID_6619	469A10	304	NA	469A10	636
OID_6933	463C7, 4 EST hits. Aligned	305	Hs.86650	AI089520	637
OID_7049	480E2	306	NA	480E2	638
IL17C	Interleukin 17C	307	Hs.278911	NM_013278	639
OID_5866	EST 3' end	308	Hs.255649	BM684739	640
CD44	CD44	309	Hs.169610	AA916990	641
VPS45A	Vacuolar protein sorting 45A (yeast)	310	Hs.6650	NM_007259	642
OID_4932	aa92c03.r1 Stratagene fetal retina 937202 cDNA clone IMAGE:838756	311	NA	AA457757	643
OID_7821	EST	312	NA	AA743221	644
OID_4916	zr76a03.r1 Soares_NhHMPu_S1 cDNA clone IMAGE:669292	313	NA	AA252909	645
OID_4891	Hypothetical protein LOC255488	314	Hs.294092	AL832329	646
HADHB	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), beta subunit	315	Hs.146812	NM_000183	647
FLJ22757	Hypothetical protein FLJ22757	316	Hs.236449	NM_024898	648
RAC1	Ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	317	Hs.173737	AK054993	649
OID_6415	72D4, FLJ00290 protein	318	Hs.98531	CA407201	650
NMES1	Normal mucosa of esophagus specific 1	319	Hs.112242	NM_032413	651
DMBT1	Deleted in malignant brain tumors 1, transcript variant 2	320	Hs.279611	NM_007329	652
RPS23	ribosomal protein S23	321	Hs.3463	NM_001025	653
ZF	HCF-binding transcription factor Zhangfei	322	Hs.29417	NM_021212	654
NFE2L3	Nuclear factor (erythroid-derived 2)-like 3	323	Hs.22900	NM_004289	655
RAD9	RAD9 homolog (S. pombe)	324	Hs.240457	NM_004584	656
OID_6295	EST 3' end	325	Hs.389327	AI880607	657
DEFCAP	Death effector filament-forming Ced-4-like apoptosis protein, transcript variant B	326	Hs.104305	NM_014922	658
RPL27A	Ribosomal protein L27a	327	Hs.76064	BF214146	659
IL22	Interleukin 22 (IL22)	328	Hs.287369	NM_020525	660

Gene	Gene Name	SEQ ID 50mer	HS	ACC	SEQ ID RNA/cDNA
PSMA4	Proteasome (prosome, macropain) subunit, alpha type, 4, (PSMA4)	329	Hs.251531	NM_002789	661
CCNI	cyclin I (CCNI)	330	Hs.79933	NM_006835	662
THBD	Thrombomodulin	331	Hs.2030	NM_000361	663
CGR19	Cell growth regulatory with ring finger domain	332	Hs.59106	NM_006568	664

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
152	CLC	Charcot-Leyden crystal protein	NM_001828	484	779	4342	
153	TERF2IP	telomeric repeat binding factor 2, interacting protein	NM_018975	485	744	1775	
154	HLA-A	Major histocompatibility complex, class I, A	NM_002116	486	735	125	1
155	OID_5891	EST 3' end	AW297949	487	730	7044.5	1
156	MSCP	mitochondrial solute carrier protein	NM_018579	488	730	3465.5	
157	DUSP5	dual specificity phosphatase 5	NM_004419	489	726	3122.5	
158	PRO1853	Hypothetical protein PRO1853	NM_018607	490	725	4153	
159	OID_6420	73A7, FLJ00290 protein	AK090404	491	725	7000.5	
160	CDSN	Corneodesmosin	NM_001264	492	722	2732	
161	OID_4269	EST	BM727677	493	715	5598.5	
162	RPS25	Ribosomal protein S25	NM_001028	494	710	164.5	
163	GAPD	Glyceraldehyde-3-phosphate dehydrogenase	NM_002046	495	707	215.5	
164	RPLP1	Ribosomal protein, large, P1	NM_001003	496	703	157	
165	OID_5115	qz23b07.x1 cDNA, 3' end /clone=IMAGE:2027701	AI364926	497	703	6629	1
166	SLC9A8	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 8	AB023156	498	702	2538.5	
167	OID_1512	IMAGE:3865861 5_clone 5'	BE618004	499	700	4008	1
168	POLR2D	Polymerase (RNA) II (DNA directed) polypeptide D	NM_004805	500	700	4190.5	
169	ARPC3	Actin related protein 2/3 complex, subunit 3, 21kDa	NM_005719	501	698	470.5	
170	OID_6282	EST 3' end	BC041913	502	697	4371.5	
171	PRO1073	PRO1073 protein	AF001542	503	697	6754	
172	OID_7222	EST, weakly similar to A43932 mucin 2 precursor, intestinal	BG260891	504	695	6759	
173	FPRL1	Formyl peptide receptor-like 1	NM_001462	505	692	4084.5	
174	FKBPL	FK506 binding protein like	NM_022110	506	691	1780.5	
175	PREB	Prolactin regulatory element binding	NM_013388	507	690	3568	
176	OID_1551	Hypothetical protein LOC200227	BE887646	508	689	6423	1
177	OID_7595	DKFZP566F0546 protein	NM_015653	509	689	3882.5	
178	RNF19	Ring finger protein 19	NM_015435	510	689	7700.5	
179	SMCY	SMC (mouse) homolog, Y chromosome (SMCY)	NM_004653	511	687	6074.5	
180	OID_4184	CMV HCMVUL109	X17403	512	687	6810.5	
181	OID_7504	Hypothetical protein FLJ35207	NM_152312	513	686	6939	
182	DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	NM_006260	514	686	3932.5	
183	ARHU	Ras homolog gene family, member U	NM_021205	515	686	7584	
184	OID_7200	Hypothetical protein FLJ22059	NM_022752	516	685	2804.5	
185	SERPINB2	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 2	NM_002575	517	684	4690.5	
186	ENO1	Enolase 1, alpha	NM_001428	518	684	327	
187	OID_7696	EST 3' end	AW297325	519	683	4875.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
188	OID_4173	CMV HCMVTRL2 (IRL2)	X17403	520	683	4010.5	
189	CSF2RB	Upstream variant mRNA of colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	AL540399	521	683	3753	
190	OID_7410	CM2-LT0042-281299-062-e11 LT0042 cDNA, mRNA sequence	AW837717	522	682	7445	
191	OID_4180	CMV HCMVUS28	X17403	523	681	4359	
192	OID_5101	EST	BG461987	524	681	7272	
193	MOP3	MOP-3	NM_018183	525	681	4085.5	1
194	RPL18A	Ribosomal protein L18a	NM_000980	526	680	238	
195	INPP5A	Inositol polyphosphate-5-phosphatase, 40kDa	NM_005539	527	680	4838.5	1
196	hIAN7	Immune associated nucleotide	BG772661	528	680	4718	
197	RPS29	Ribosomal protein S29	NM_001032	529	680	107.5	
198	OID_6008	EST 3' end	AW592876	530	679	6560.5	
199	OID_4186	CMV HCMVUL122	X17403	531	677	4788.5	
200	VNN2	vanin 2	NM_004665	532	677	2620.5	
201	OID_7703	KIAA0907 protein	NM_014949	533	676	6104.5	
202	OID_7057	480F8	480F8	534	675	6862	
203	OID_4291	EST	BC038439	535	674	5618.5	
204	OID_1366	EST	AW850041	536	674	5590.5	1
205	EEF1A1	Eukaryotic translation elongation factor 1 alpha 1	NM_001402	537	672	232	
206	PA2G4	Proliferation-associated 2G4, 38kDa	NM_006191	538	672	4402	
207	GAPD	Glyceraldehyde-3-phosphate dehydrogenase	NM_002046	539	671	194.5	
208	CHD4	Chromodomain helicase DNA binding protein 4	NM_001273	540	671	2578.5	
209	OID_7951	E2F-like protein (LOC51270)	NM_016521	541	671	4467	
210	DAB1	Disabled homolog 1 (Drosophila)	NM_021080	542	670	6357.5	
211	OID_3406	Hypothetical protein FLJ20356	NM_018986	543	669	2087	
212	OID_6986	462H9 EST	AK093608	544	669	4454	1
213	OID_5962	EST 3' end	AW452467	545	668	5870.5	1
214	OID_5152	EST 3' end	AI392805	546	668	6354.5	
215	S100A8	S100 calcium-binding protein A8 (calgranulin A)	NM_002964	547	668	134	
216	HNRPU	HNRPU Heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)	BM467823	548	668	4108	
217	ERCC5	Excision repair cross-complementing rodent repair deficiency, complementation group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome))	NM_000123	549	668	6430.5	
218	RPS27	Ribosomal protein S27 (metallopanstimulin 1)	NM_001030	550	668	160	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
219	ACRC	acidic repeat containing (ACRC),	NM_052957	551	668	4871.5	1
220	PSMD11	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	AI684022	552	668	4138	
221	OID_1016	FLJ00048 protein	AK024456	553	667	5199	
222	OID_1309	AV706481 cDNA	AV706481	554	667	7279.5	
223	OID_7582	Weakly similar to ZINC FINGER PROTEIN 142	AK027866	555	667	5003.5	1
224	OID_4317	ta73c09.x1 3' end /clone=IMAGE:2049712 Ribosomal Protein S15	AI318342	556	667	6499	
225	OID_5889	3' end /clone=IMAGE:3083913	AW297843	557	666	6837	1
226	UBL1	Ubiquitin-like 1 (sentrin)	NM_003352	558	666	1978.5	
227	OID_3687	EST	W03955	559	666	5519.5	
228	OID_7371	EST 5'	BE730505	560	665	7751.5	
229	SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	NM_031286	561	665	310	
230	SEMA7A	Sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	NM_003612	562	665	3505.5	
231	OID_5708	EST 3' end	AW081540	563	665	6224.5	
232	OID_5992	EST 3' end	AW467992	564	665	5648	
233	IL21	Interleukin 21	NM_021803	565	664	5036.5	
234	HERC3	Hect domain and RLD 3 (HERC3)	NM_014606	566	664	3056.5	1
235	OID_7799	AluJo/FLAM SINE/Alu	AW837717	567	664	3544	
236	P11	26 serine protease	NM_006025	568	664	7173	
237	OID_7766	EST 3' end	AW294711	569	663	7270.5	
238	TIMM10	translocase of inner mitochondrial membrane 10 (yeast) homolog (TIMM10)	NM_012456	570	663	4779.5	
239	EGLN1	Egl nine homolog 1 (C. elegans)	AJ310543	571	662	7172.5	
240	TBCC	Tubulin-specific chaperone c	NM_003192	572	662	3384	
241	RNF3	Ring finger protein 3	NM_006315	573	661	4062	
242	OID_6451	170F9, hypothetical protein FLJ21439	AL834168	574	661	7126	1
243	CCNDBP1	cyclin D-type binding-protein 1 (CCNDBP1)	NM_012142	575	661	1919	
244	OID_8063	MUC18 gene exons 1&2	X68264	576	661	4692.5	
245	SUV39H1	Suppressor of variegation 3-9 homolog 1 (Drosophila)	NM_003173	577	661	5103	1
246	HSPC048	HSPC048 protein	NM_014148	578	660	5981.5	
247	OID_5625	EST 3' end from T cells	AW063780	579	660	4437	1
248	WARS	Tryptophanyl-tRNA synthetase	NM_004184	580	660	905.5	
249	OID_6823	107H8	AL832642	581	659	2619	
250	OID_7073	119F12	AL705961	582	659	6837.5	
251	OID_5339	EST 3' end	AI625119	583	658	4414.5	1
252	OID_4263	fetal retina 937202 cDNA clone IMAGE:565899	AA136584	584	658	5870	
253	MGC26766	Hypothetical protein MGC26766	AK025472	585	658	1892.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
254	SERPINB11	Serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 11	NM_080475	586	658	7535.5	1
255	OID_6711	58G4, IMAGE:4359351 5'	BF968628	587	658	7264	
256	RNF10	Ring finger protein 10	NM_014868	588	658	3127.5	
257	MKRN1	Makorin, ring finger protein, 1	NM_013446	589	658	2228.5	
258	RPS16	ribosomal protein S16	NM_001020	590	657	165.5	
259	BAZ1A	Bromodomain adjacent to zinc finger domain, 1A	NM_013448	591	657	2533	
260	OID_5998	EST 3' end	AW468459	592	657	6339.5	
261	ATP5L	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g	NM_006476	593	657	1155	
262	OID_6393	52B9	52B9	594	657	7420.5	
263	RoXaN	Ubiquitous tetratricopeptide containing protein RoXaN	BC004857	595	656	7378	
264	NCBP2	Nuclear cap binding protein subunit 2, 20kDa	NM_007362	596	656	4666.5	
265	OID_6273	EST 3' end	AW294774	597	656	5498.5	
266	HZF12	zinc finger protein 12	NM_033204	598	656	4715.5	
267	CCL3	Chemokine (C-C motif) ligand 3	D90144	599	656	4910	1
268	OID_4323	IMAGE:1283731 3'	AA744774	600	655	6406.5	1
269	OID_5181	tg93h12.x1 NCI_CGAP_CLL1 cDNA clone IMAGE:2116391 3' similar to contains TAR1.t1 MER22	AI400725	601	655	4838	1
270	PRDX4	Peroxiredoxin 4	NM_006406	602	655	3397.5	
271	BTK	Bruton agammaglobulinemia tyrosine kinase	NM_000061	603	655	2358	
272	OID_6298	Importin beta subunit mRNA	AI948513	604	655	2433.5	
273	PGK1	Phosphoglycerate kinase 1	NM_000291	605	655	2059.5	
274	TNFRSF10A	Tumor necrosis factor receptor superfamily, member 10a	NM_003844	606	654	4897.5	1
275	ADM	adrenomedullin	NM_001124	607	654	4235	
276	OID_357	138G5	138G5	608	654	5427.5	1
277	C20orf6	461A4 chromosome 20 open reading frame 6	NM_016649	609	654	6343	1
278	OID_3226	DKFZP564O0823 protein	NM_015393	610	653	6187.5	
279	ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	NM_004315	611	653	1003	
280	ATF5	Activating transcription factor 5	NM_012068	612	653	4545.5	
281	OID_4887	hypothetical protein MGC14376	NM_032895	613	653	2310	1
282	OID_4239	EST	BQ022840	614	652	2774.5	
283	MDM2	Mouse double minute 2, homolog of; p53-binding protein (MDM2), transcript variant MDM2,	NM_002392	615	652	4342	
284	XRN2	5'-3' exoribonuclease 2	AF064257	616	652	6896.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
285	OID_6039	Endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 4 (EDG4)	BE502246	617	652	5147	
286	OID_4210	IMAGE:4540096	AI300700	618	652	1330.5	
287	OID_7698	EST 3' end	AA243283	619	652	7432.5	1
288	PRKRA	Protein kinase, interferon-inducible double stranded RNA dependent activator	NM_003690	620	652	3512.5	
289	OID_4288	IMAGE:2091815	AI378046	621	651	6401.5	
290	OID_5620	EST 3' end from T cells	AW063678	622	651	6400	
291	OID_7384	EST 5'	BF475239	623	651	6875	
292	OID_1209	EST Weakly similar to hypothetical protein FLJ20378	C14379	624	651	1356.5	1
293	CDKN1B	Cyclin-dependent kinase inhibitor 1B (p27, Kip1)	NM_004064	625	650	4272.5	
294	PLOD	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase, Ehlers-Danlos syndrome type VI)	NM_000302	626	650	3101	
295	OID_5128	EST	AK097845	627	650	6476	
296	OID_5877	EST 3' end	AW297664	628	650	6864.5	1
297	FZD4	Frizzled (Drosophila) homolog 4	NM_012193	629	650	5816	
298	HLA-B	Major histocompatibility complex, class I, B	NM_005514	630	650	229	
299	OID_5624	EST 3' end from T cells	AW063921	631	649	7812.5	
300	FPR1	Formyl peptide receptor 1	NM_002029	632	649	1156.5	
301	ODF2	Outer dense fiber of sperm tails 2	NM_153437	633	649	4982.5	
302	OID_5150	tg04g01.x1 cDNA, 3' end /clone=IMAGE:2107824	AI392793	634	649	7638	
303	OID_5639	EST 3' end from T cells	AW064243	635	648	6805	1
304	OID_6619	469A10	469A10	636	647	7110	1
305	OID_6933	463C7, 4 EST hits. Aligned	AI089520	637	647	6880.5	1
306	OID_7049	480E2	480E2	638	647	7128.5	
307	IL17C	Interleukin 17C	NM_013278	639	647	6411.5	
308	OID_5866	EST 3' end	BM684739	640	647	6532	1
309	CD44	CD44	AA916990	641	646	4758	
310	VPS45A	Vacuolar protein sorting 45A (yeast)	NM_007259	642	646	3371	
311	OID_4932	aa92c03.r1 Stratagene fetal retina 937202 cDNA clone IMAGE:838756	AA457757	643	646	6057	1
312	OID_7821	EST	AA743221	644	645	7507	
313	OID_4916	zr76a03.r1 Soares_NhHMPu_S1 cDNA clone IMAGE:669292	AA252909	645	645	6962.5	1
314	OID_4891	Hypothetical protein LOC255488	AL832329	646	645	6148.5	

SEQ ID 50mer	Gene	Gene Name	ACC	SEQ ID RNA/cDNA	Non-Para Score	Median Rank in NR	Down Regulated
315	HADHB	Hydroxyacyl-Coenzyme A dehydrogenase/3-ketoacyl-Coenzyme A thiolase/enoyl-Coenzyme A hydratase (trifunctional protein), beta subunit	NM_000183	647	645	3212.5	
316	FLJ22757	Hypothetical protein FLJ22757	NM_024898	648	644	1965.5	1
317	RAC1	Ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	AK054993	649	644	1533	
318	OID_6415	72D4, FLJ00290 protein	CA407201	650	644	4881	
319	NMES1	Normal mucosa of esophagus specific 1	NM_032413	651	644	6217	1
320	DMBT1	Deleted in malignant brain tumors 1, transcript variant 2	NM_007329	652	644	7284	
321	RPS23	ribosomal protein S23	NM_001025	653	643	219.5	
322	ZF	HCF-binding transcription factor Zhangfei	NM_021212	654	643	4069	
323	NFE2L3	Nuclear factor (erythroid-derived 2)-like 3	NM_004289	655	643	3378	
324	RAD9	RAD9 homolog (S. pombe)	NM_004584	656	643	6453	
325	OID_6295	EST 3' end	AI880607	657	643	7493.5	
326	DEFCAP	Death effector filament-forming Ced-4-like apoptosis protein, transcript variant B	NM_014922	658	643	3059	
327	RPL27A	Ribosomal protein L27a	BF214146	659	642	6571	1
328	IL22	Interleukin 22 (IL22)	NM_020525	660	642	3891	1
329	PSMA4	Proteasome (prosome, macropain) subunit, alpha type, 4, (PSMA4)	NM_002789	661	641	1934.5	
330	CCNI	cyclin I (CCNI)	NM_006835	662	641	980.5	
331	THBD	Thrombomodulin	NM_000361	663	640	4732.5	
332	CGR19	Cell growth regulatory with ring finger domain	NM_006568	664	640	5510	

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
HSRRN18S	1	333	665	996	1327			
ACTB	2	334	666	997	1328			
GUSB	3	335	667	998	1329	1656	1904	2152
B2M	4	336	668	999	1330			
TSN	5	337	669	1000	1331	1657	1905	2153
CCR7	6	338	670	1001	1332			
IL1R2	7	339	671	1002	1333	1658	1906	2154
AIF-1	8	340	672	1003	1334			
ALAS2	9	341	673	1004	1335			
APELIN	10	342	674	1005	1336			
CD80	11	343	675	1006	1337	1659	1907	2145
EPB41	12	344	676	1007	1338			
CBLB	13	345	677	1008	1339	1660	1908	2156
CCR5	14	346	678	1009	1340	1661	1909	2157
MME	15	347	679	1010	1341	1662	1910	2158
KLRC1	16	348	680	1011	1342	1663	1911	2159
FCGR3A	17	349	681	1012	1343			
FCGR3B	18	350	682	1013	1344	1664	1912	2160
LAG3	19	351	683	1014	1345	1665	1913	2161
PECAM1	20	352	684	1015	1346	1666	1914	2162
CD34	21	353	685	1016	1347	1667	1915	2163
FCGR1A	22	354	686	1017	1348	1668	1916	2164
TFRC	23	355	687	1018	1349			
CMA1	24	356	688	1019	1350	1669	1917	2165
KIT	25	357	689	1020	1351			
MPL	26	358	690	1021	1352	1670	1918	2166
EphB6	27	359	691	1022	1353			
EPO-R	28	360	692	1023	1354			
Foxp3	29	361	693	1024	1355	1671	1919	2167
GATA-1	30	362	694	1025	1356			
ITGA2B	31	363	695	1026	1357	1672	1920	2168
GNLY	32	364	696	1027	1358	1673	1921	2169
GZMA	33	365	697	1028	1359	1674	1922	2170
HBA	34	366	698	1029	1360	1675	1923	2171
HBZ	35	367	699	1030	1361	1676	1924	2172
HBB	36	368	700	1031	1362	1677	1925	2173
HBD	37	369	701	1032	1363	1678	1926	2174
HBE	38	370	702	1033	1364	1679	1927	2175
HBG	39	371	703	1034	1365	1680	1928	2176
HBQ	40	372	704	1035	1366	1681	1929	2177
HLA-DP	41	373	705	1036	1367	1682	1930	2178
HLA-DQ	42	374	706	1037	1368	1683	1931	2179
HLA-DRB	43	375	707	1038	1369	1684	1932	2180
ICOS	44	376	708	1039	1370	1685	1933	2181
IL18	45	377	709	1040	1371	1686	1934	2182
IL3	46	378	710	1041	1372	1687	1935	2183
ITGA4	47	379	711	1042	1373			
ITGAM	48	380	712	1043	1374	1688	1936	2184
ITGB7	49	381	713	1044	1375			
CEBPB	50	382	714	1045	1376	1689	1937	2185
NF-E2	51	383	715	1046	1377			
PDCD1	52	384	716	1047	1378	1690	1938	2186
PF4	53	385	717	1048	1379	1691	1939	2187
PRKCQ	54	386	718	1049	1380	1692	1940	2188
PPARGC1	55	387	719	1050	1381			

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
RAG1	56	388	720	1051	1382	1693	1941	2189
RAG2	57	389	721	1052	1383	1694	1942	2190
CXCL12	58	390	722	1053	1384	1695	1943	2191
TNFRSF4	59	391	723	1054	1385	1696	1944	2192
TNFSF4	60	392	724	1055	1386	1697	1945	2193
TPS1	61	393	725	1056	1387	1698	1946	2194
ADA	62	394	726	1057	1388	1699	1947	2195
CPM	63	395	727	1058	1389	1700	1948	2196
CSF2	64	396	728	1059	1390	1701	1949	2197
CSF3	65	397	729	1060	1391	1702	1950	2198
CRP	66	398	730	1061	1392	1703	1951	2199
FLT3	67	399	731	1062	1393	1704	1952	2200
GATA3	68	400	732	1063	1394	1705	1953	2201
IL7R	69	401	733	1064	1395	1706	1954	2202
KLF1	70	402	734	1065	1396	1707	1955	2203
LCK	71	403	735	1066	1397	1708	1956	2204
LEF1	72	404	736	1067	1398	1709	1957	2205
PLAUR	73	405	737	1068	1399	1710	1958	2206
TNFSF13B	74	406	738	1069	1400	1711	1959	2207
IL8	75	407	739	1070	1401			
GZMB	76	408	740	1071	1402			
TNFSF6	77	409	741	1072	1403			
TCIRG1	78	410	742	1073	1404			
PRF1	79	411	743	1074	1405			
IL4	80	412	744	1075	1406			
IL13	81	413	745	1076	1407			
CTLA4	82	414	746	1077	1408			
CD8A	83	415	747	1078	1409			
BY55	84	416	748	1079	1410			
OID_4460	85	417	749	1080	1411			
HBB	86	418	750	1081	1412			
BPGM	87	419	751	1082	1413			
MTHFD2	88	420	752	1083	1414			
TAP1	89	421	753	1084	1415			
KPNA6	90	422	754	1085	1416			
OID_4365	91	423	755	1086	1417			
IGHM	92	424	756	1087	1418			
OID_573	93	425	757	1088	1419	1712	1960	2208
OID_873	94	426	758	1089	1420			
OID_3	95	427	759	1090	1421			
CXCR4	96	428	760	1091	1422			
CD69	97	429	761	1092	1423			
CCL5	98	430	762	1093	1424			
IL6	99	431	763	1094	1425			
IL2	100	432	764	1095	1426			
KLRF1	101	433	765	1096	1427			
LYN	102	434	766	1097	1428			
IL2RA	103	435	767	1098	1429			
CCL4	104	436	768	1099	1430			
OID_6207	105	437	769	1100	1431			
ChGn	106	438	770	1101	1432			
OID_4281	107	439	771	1102	1433			
CXCL9	108	440	772	1103	1434			
CXCL10	109	441	773	1104	1435			
IL17	110	442	774	1105	1436			

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
IL15	111	443	775	1106	1437			
IL10	112	444	776	1107	1438			
IFNG	113	445	777	1108	1439	1713	1961	2209
HLA-DRB1	114	446	778	1109	1440	1714	1962	2210
CD8B1	115	447	779	1110	1441			
CD4	116	448	780	1111	1442			
CXCR3	117	449	781	1112	1443			
OID_7094	118	450	782	1113	1444			
OID_7605	119	451	783	1114	1445			
CXCL1	120	452	784	1115	1446			
OID_253	121	453	785	1116	1447			
GPI	122	454	786	1117	1448			
CD47	123	455	787	1118	1449			
HLA-F	124	456	788	1119	1450			
OID_5350	125	457	789	1120	1451			
TCRGC2	126	458	790	1121	1452			
OID_7016	127	459	791	1122				
PTGS2	128	460	792	1123	1454			
OID_5847	129	461	793	1124	1455			
PRDM1	130	462	794	1125	1456			
CKB	131	463	795	1126	1457			
TNNI3	132	464	796	1127	1458			
TNNT2	133	465	797	1128	1459			
MB	134	466	798	1129	1460			
SLC7A11	135	467	799	1130	1461			
TNFRSF5	136	468	800	1131	1462	1715	1963	2211
TNFRSF7	137	469	801	1132	1463			
CD86	138	470	802	1133	1464			
AIF1v2	139	471	803	1134	1465			
EV BCLF-1	140	472	804	1135	1466	1716	1964	2212
EV EBV	141	473	805	1136	1467	1717	1965	2213
CMV p67	142	474	806	1137	1468	1718	1966	2214
CMV TRL7	143	475	807	1138	1469	1719	1967	2215
CMV IE1e3	144	476	808	1139	1470	1720	1968	2216
CMV IE1e4	145	477	809	1140	1471	1721	1969	2217
EV EBNA-1	146	478	810	1141	1472	1722	1970	2218
EV BZLF-1	147	479	811	1142	1473	1723	1971	2219
EV EBN	148	480	812	1143	1474	1724	1972	2220
EV EBNA-L	149	481	813	1144	1475			
CMV IE1	150	482	814	1145	1476	1725	1973	2221
CMV IE1	151	483	815	1146	1477			
CLC	152	484	816	1147	1478	1726	1974	2222
TERF2IP	153	485	817	1148	1479	1727	1975	2223
HLA-A	154	486	818	1149	1480	1728	1976	2224
OID_5891	155	487	819	1150	1481	1729	1977	2225
MSCP	156	488	820	1151	1482	1730	1978	2226
DUSP5	157	489	821	1152	1483	1731	1979	2227
PRO1853	158	490	822	1153	1484	1732	1980	2228
OID_6420	159	491	823	1154	1485	1733	1981	2229
CDSN	160	492	824	1155	1486	1734	1982	2230
OID_4269	161	493	825	1156	1487	1735	1983	2231
RPS25	162	494	826	1157	1488	1736	1984	2232
GAPD	163	495	827	1158	1489	1737	1985	2233
RPLP1	164	496	828	1159	1490	1738	1986	2234
OID_5115	165	497	829	1160	1491	1739	1987	2235

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
SLC9A8	166	498	830	1161	1492	1740	1988	2236
OID_1512	167	499	831	1162	1493	1741	1989	2237
POLR2D	168	500	832	1163	1494	1742	1990	2238
ARPC3	169	501	833	1164	1495	1743	1991	2239
OID_6282	170	502	834	1165	1496	1744	1992	2240
PRO1073	171	503	835	1166	1497	1745	1993	2241
OID_7222	172	504	836	1167	1498	1746	1994	2242
FPRL1	173	505	837	1168	1499	1747	1995	2243
FKBPL	174	506	838	1169	1500	1748	1996	2244
PREB	175	507	839	1170	1501	1749	1997	2245
OID_1551	176	508	840	1171	1502	1750	1998	2246
OID_7595	177	509	841	1172	1503	1751	1999	2247
RNF19	178	510	842	1173	1504	1752	2000	2248
SMCY	179	511	843	1174	1505	1753	2001	2249
OID_4184	180	512	844	1175	1506	1754	2002	2250
OID_7504	181	513	845	1176	1507	1755	2003	2251
DNAJC3	182	514	846	1177	1508	1756	2004	2252
ARHU	183	515	847	1178	1509	1757	2005	2253
OID_7200	184	516	848	1179	1510	1758	2006	2254
SERPINB2	185	517	849	1180	1511			
ENO1	186	518	850	1181	1512	1759	2007	2255
OID_7696	187	519	851	1182	1513	1760	2008	2256
OID_4173	188	520	852	1183	1514	1761	2009	2257
CSF2RB	189	521	853	1184	1515	1762	2010	2258
OID_7410	190	522	854	1185	1516	1763	2011	2259
OID_4180	191	523	855	1186	1517	1764	2012	2260
OID_5101	192	524	856	1187	1518	1765	2013	2261
MOP3	193	525	857	1188	1519	1766	2014	2262
RPL18A	194	526	858	1189	1520	1767	2015	2263
INPP5A	195	527	859	1190	1521	1768	2016	2264
hIAN7	196	528	860	1191	1522	1769	2017	2265
RPS29	197	529	861	1192	1523	1770	2018	2266
OID_6008	198	530	862	1193	1524	1771	2019	2267
OID_4186	199	531	863	1194	1525	1772	2020	2268
VNN2	200	532	864	1195	1526	1773	2021	2269
OID_7703	201	533	865	1196	1527	1774	2022	2270
OID_7057	202	534	866	1197	1528	1775	2023	2271
OID_4291	203	535	867	1198	1529	1776	2024	2272
OID_1366	204	536	868	1199	1530	1777	2025	2273
EEF1A1	205	537	869	1200	1531	1778	2026	2274
PA2G4	206	538	870	1201	1532	1779	2027	2275
GAPD	207	539	871	1202	1533	1780	2028	2276
CHD4	208	540	872	1203	1534	1781	2029	2277
OID_7951	209	541	873	1204	1535	1782	2030	2278
DAB1	210	542	874	1205	1536	1783	2031	2279
OID_3406	211	543	875	1206	1537	1784	2032	2280
OID_6986	212	544	876	1207	1538	1785	2033	2281
OID_5962	213	545	877	1208	1539	1786	2034	2282
OID_5152	214	546	878	1209	1540	1787	2035	2283
S100A8	215	547	879	1210	1541	1788	2036	2284
HNRPU	216	548	880	1211	1542	1789	2037	2285
ERCC5	217	549	881	1212	1543	1790	2038	2286
RPS27	218	550	882	1213	1544	1791	2039	2287
ACRC	219	551	883	1214	1545	1792	2040	2288
PSMD11	220	552	884	1215	1546	1793	2041	2289

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
OID_1016	221	553	885	1216	1547	1794	2042	2290
OID_1309	222	554	886	1217	1548	1795	2043	2291
OID_7582	223	555	887	1218	1549	1796	2044	2292
OID_4317	224	556	888	1219	1550	1797	2045	2293
OID_5889	225	557	889	1220	1551	1798	2046	2294
UBL1	226	558	890	1221	1552	1799	2047	2295
OID_3687	227	559	891	1222	1553	1800	2048	2296
OID_7371	228	560	892	1223	1554	1801	2049	2297
SH3BGRL3	229	561	893	1224	1555	1802	2050	2298
SEMA7A	230	562	894	1225	1556	1803	2051	2299
OID_5708	231	563	895	1226	1557	1804	2052	2300
OID_5992	232	564	896	1227	1558	1805	2053	2301
IL21	233	565	897	1228	1559	1806	2054	2302
HERC3	234	566	898	1229	1560	1807	2055	2303
OID_7799	235	567	899	1230	1561	1808	2056	2304
P11	236	568	900	1231	1562	1809	2057	2305
OID_7766	237	569	901	1232	1563	1810	2058	2306
TIMM10	238	570	902	1233	1564	1811	2059	2307
EGLN1	239	571	903	1234	1565	1812	2060	2308
TBCC	240	572	904	1235	1566	1813	2061	2309
RNF3	241	573	905	1236	1567	1814	2062	2310
OID_6451	242	574	906	1237	1568	1815	2063	2311
CCNDBP1	243	575	907	1238	1569	1816	2064	2312
OID_8063	244	576	908	1239	1570	1817	2065	2313
SUV39H1	245	577	909	1240	1571	1818	2066	2314
HSPC048	246	578	910	1241	1572	1819	2067	2315
OID_5625	247	579	911	1242	1573	1820	2068	2316
WARS	248	580	912	1243	1574	1821	2069	2317
OID_6823	249	581	913	1244	1575	1822	2070	2318
OID_7073	250	582	914	1245	1576	1823	2071	2319
OID_5339	251	583	915	1246	1577	1824	2072	2320
OID_4263	252	584	916	1247	1578	1825	2073	2321
MGC26766	253	585	917	1248	1579	1826	2074	2322
SERPINB11	254	586	918	1249	1580	1827	2075	2323
OID_6711	255	587	919	1250	1581	1828	2076	2324
RNF10	256	588	920	1251	1582	1829	2077	2325
MKRN1	257	589	921	1252	1583	1830	2078	2326
RPS16	258	590	922	1253	1584	1831	2079	2327
BAZ1A	259	591	923	1254	1585	1832	2080	2328
OID_5998	260	592	924	1255	1586	1833	2081	2329
ATP5L	261	593	925	1256	1587	1834	2082	2330
OID_6393	262	594	926	1257	1588			
RoXaN	263	595	927	1258	1589	1835	2083	2331
NCBP2	264	596	928	1259	1590	1836	2084	2332
OID_6273	265	597	929	1260	1591	1837	2085	2333
HZF12	266	598	930	1261	1592	1838	2086	2334
CCL3	267	599	931	1262	1593	1839	2087	2335
OID_4323	268	600	932	1263	1594	1840	2088	2336
OID_5181	269	601						
PRDX4	270	602	933	1264	1595	1841	2089	2337
BTK	271	603	934	1265	1596	1842	2090	2338
OID_6298	272	604	935	1266	1597	1843	2091	2339
PGK1	273	605	936	1267	1598	1844	2092	2340
TNFRSF10A	274	606	937	1268	1599	1845	2093	2341
ADM	275	607	938	1269	1600	1846	2094	2342

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
OID_357	276	608	939	1270	1601	1847	2095	2343
C20orf6	277	609	940	1271	1602	1848	2096	2344
OID_3226	278	610	941	1272	1603	1849	2097	2345
ASAH1	279	611	942	1273	1604	1850	2098	2346
ATF5	280	612	943	1274	1605	1851	2099	2347
OID_4887	281	613	944	1275	1606	1852	2100	2348
OID_4239	282	614	945	1276	1607	1853	2101	2349
MDM2	283	615	946	1277	1608	1854	2102	2350
XRN2	284	616	947	1278	1609	1855	2103	2351
OID_6039	285	617	948	1279	1610	1856	2104	2352
OID_4210	286	618	949	1280	1611	1857	2105	2353
OID_7698	287	619	950	1281	1612	1858	2106	2354
PRKRA	288	620	951	1282	1613	1859	2107	2355
OID_4288	289	621	952	1283	1614	1860	2108	2356
OID_5620	290	622	953	1284	1615	1861	2109	2357
OID_7384	291	623	954	1285	1616	1862	2110	2358
OID_1209	292	624	955	1286	1617	1863	2111	2359
CDKN1B	293	625	956	1287	1618	1864	2112	2360
PLOD	294	626	957	1288	1619	1865	2113	2361
OID_5128	295	627	958	1289	1620	1866	2114	2362
OID_5877	296	628	959	1290	1621	1867	2115	2363
FZD4	297	629	960	1291	1622	1868	2116	2364
HLA-B	298	630	961	1292	1623	1869	2117	2365
OID_5624	299	631	962	1293	1624	1870	2118	2366
FPR1	300	632	963	1294	1625	1871	2119	2367
ODF2	301	633	964	1295	1626	1872	2120	2368
OID_5150	302	634	965	1296	1627	1873	2121	2369
OID_5639	303	635	966	1297	1628	1874	2122	2370
OID_6619	304	636	967	1298	1629	1875	2123	2371
OID_6933	305	637	968	1299	1630	1876	2124	2372
OID_7049	306	638	969	1300	1631	1877	2125	2373
IL17C	307	639	970	1301	1632	1878	2126	2374
OID_5866	308	640	971	1302	1633	1879	2127	2375
CD44	309	641	972	1303	1634	1880	2128	2376
VPS45A	310	642	973	1304	1635	1881	2129	2377
OID_4932	311	643	974	1305	1636	1882	2130	2378
OID_7821	312	644	975	1306	1637	1883	2131	2379
OID_4916	313	645	976	1307	1638	1884	2132	2380
OID_4891	314	646	977	1308	1639	1885	2133	2381
HADHB	315	647	978	1309	1640	1886	2134	2382
FLJ22757	316	648	979	1310	1641	1887	2135	2383
RAC1	317	649	980	1311	1642	1888	2136	2384
OID_6415	318	650	981	1312	1643	1889	2137	2385
NMES1	319	651	982	1313	1644	1890	2138	2386
DMBT1	320	652	983	1314	1645	1891	2139	2387
RPS23	321	653	984	1315	1646	1892	2140	2388
ZF	322	654	985	1316	1647	1893	2141	2389
NFE2L3	323	655	986	1317	1648	1894	2142	2390
RAD9	324	656	987	1318	1649	1895	2143	2391
OID_6295	325	657	988	1319	1650	1896	2144	2392
DEFCAP	326	658	989	1320	1651	1897	2145	2393
RPL27A	327	659	990	1321	1652	1898	2146	2394
IL22	328	660	991	1322	1653	1899	2147	2395
PSMA4	329	661	992	1323	1654	1900	2148	2396
CCNI	330	662	993	1324	1655	1901	2149	2397

Gene	SEQ ID 50mer	SEQ ID RNA/cDNA	PCR Forward Primer 1 SEQ ID	PCR Reverse Primer 1 SEQ ID	PCR Probe 1 SEQ ID	PCR Forward Primer 2 SEQ ID	PCR Reverse Primer 2 SEQ ID	PCR Probe 2 SEQ ID
THBD	331	663	994	1325	1656	1902	2150	2398
CGR19	332	664	995	1326	1657	1903	2151	2399

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
HBB	Hemoglobin, beta	86	418	55	8.33	0.00	0.00
OID_4365	Mitochondrial solute carrier	91	423	53	6.16	0.00	0.00
OID_873	KIAA1892 protein	94	426	55	5.09	0.01	0.01
IL4	Interleukin 4	80	412	46	4.90	0.02	0.01
OID_4281	EST	107	439	56	5.19	0.01	0.01
IGHM	Immunoglobulin heavy constant mu	92	424	52	2.89	0.09	0.01
BPGM	2,3-bisphosphoglycerate mutase	87	419	43	7.31	0.01	0.01
CTLA4	Cytotoxic T-lymphocyte-associated protein 4	82	414	52	1.84		0.02
SLC7A11	Solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	135	467	48	2.50	0.15	0.03
IL13	Interleukin 13	81	413	29	4.95	0.07	0.04
OID_6207	EST	105	437	37	3.58	0.10	0.04
PRDM1	PR domain containing 1, with ZNF domain	130	462	57	1.44		0.07
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	102	434	55	1.08		0.08
KPNA6	Karyopherin alpha 6 (importin alpha 7)	90	422	51	1.50		0.09
OID_7094	XDx EST 479G12	118	450	35	1.13		0.09
IL15	Interleukin 15	111	443	51	3.78	0.05	0.09
OID_4460	EST	85	417	47	2.73	0.14	0.10
OID_7016	EST	127	459	53	2.14	0.27	0.10
MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	88	420	43	3.50	0.07	0.11
TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	78	410	57	1.08		0.11
OID_5847	Hypothetical protein FLJ32919	129	461	45	1.08		0.12
CXCR4	Chemokine (C-X-C motif	96	428	56	1.29		0.12
CXCR3	Chemokine (C-X-C motif	117	449	54	2.10	0.27	0.12
GPI	Glucose phosphate isome	122	454	57	1.44	0.60	0.12
KLRF1	Killer cell lectin-like rece	101	433	50	1.68		0.13
CCL5	Chemokine (C-C motif) l	98	430	34	1.96		0.13
CD47	CD47 antigen (Rh-related	123	455	55	1.45		0.13
IL10	Interleukin 10	112	444	33	1.43		0.13
OID_253	EST	121	453	26	1.93		0.15
CXCL10	Chemokine (C-X-C motif	109	441	53	1.75		0.16

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
IFNG	Interferon, gamma	113	445	41	1.33		0.16
PRF1	Perforin 1 (pore forming	79	411	48	1.20		0.17
IL2	Interleukin 2	100	432	33	2.00		0.17
HLA-DRB1	Major histocompatibility	114	446	42	1.50		0.18
IL6	Interleukin 6	99	431	49	1.33		0.18
IL2RA	Interleukin 2 receptor, alpha	103	435	39	2.03	0.34	0.19
OID_573	KIAA1486 protein	93	425	8	3.00		0.19
CXCL9	Chemokine (C-X-C motif) ligand 9 (MIG)	108	440	46	1.71		0.20
OID_3	EST	95	427	49	2.19		0.20
CD8B1	CD8 antigen, beta polypeptide 1 (p37)	115	447	55	1.21		0.22
CD69	CD69 antigen (p60, early T-cell activation antigen)	97	429	30	1.71		0.23
OID_7605	EST	119	451	47	3.11	0.08	0.24
TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	77	409	54	1.36		0.25
CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	120	452	20	2.00		0.26
OID_5350	EST	125	457	49	2.08	0.26	0.28
CD8A	CD8 antigen, alpha polypeptide (p32)	83	415	57	1.39		0.28
CD4	CD4 antigen (p55)	116	448	55	1.64		0.28
PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	128	460	46	2.05	0.37	0.29
GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	76	408	40	1.81		0.33
CCL4	Chemokine (C-C motif) ligand 4, SCYA4	104	436	53	2.25		0.35
ChGn	Chondroitin beta 1,4 N-acetylgalactosaminyltransferase	106	438	31	2.57		0.36
TCRGC2	T cell receptor gamma constant 2	126	458	52	1.33		0.39
HLA-F	Major histocompatibility complex, class I, F	124	456	54	2.36	0.17	0.40
TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	89	421	36	1.93		0.45

Gene	Gene Name	SEQ ID 50mer	SEQ ID RNA/cDNA	n	Non-parametric Odds ratio	Fisher p-value	t-test p-value
BY55	Natural killer cell receptor, immunoglobulin superfamily member	84	416	52	2.49	0.16	0.48
IL8	Interleukin 8	75	407	49	2.10	0.26	0.49

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
ACTB	NM_001101	2	334	NP_001092	2400
GUSB	NM_000181	3	335	NP_000172	2401
B2M	NM_004048	4	336	NP_004039	2402
TSN	NM_004622	5	337	NP_004613	2403
CCR7	NM_001838	6	338	NP_001829	2404
IL1R2	NM_004633	7	339	NP_004624	2405
AIF-1	NM_004847	8	340	NP_004838	2406
ALAS2	NM_000032.1	9	341	NP_000023	2407
APELIN	NM_017413	10	342	NP_059109	2408
CD80	NM_005191	11	343	NP_005182	2409
EPB41	NM_004437	12	344	NP_004428	2410
CBLB	NM_004351	13	345	NP_733762	2411
CCR5	NM_000579	14	346	NP_000570	2412
MME	NM_000902	15	347	NP_000893	2413
KLRC1	NM_002259	16	348	NP_002250	2414
FCGR3A	NM_000569	17	349	NP_000560	2415
FCGR3B	NM_000570	18	350	NP_000561	2416
LAG3	NM_002286	19	351	NP_002277	2417
PECAM1	NM_000442	20	352	NP_000433	2418
CD34	NM_001773	21	353	NP_001764	2419
FCGR1A	NM_000566	22	354	NP_000557	2420
TFRC	NM_003234	23	355	NP_003225	2421
CMA1	NM_001836	24	356	NP_001827	2422
KIT	NM_000222	25	357	NP_000213	2423
MPL	NM_005373	26	358	NP_005364	2424
EphB6	NM_004445	27	359	NP_004436	2425
EPO-R	NM_000121.2	28	360	NP_000112	2426
Foxp3	NM_014009	29	361	NP_054728	2427
GATA-1	NM_002049	30	362	NP_002040	2428
ITGA2B	NM_000419	31	363	NP_000410	2429
GNLY	NM_006433	32	364	NP_006424	2430
GZMA	NM_006144	33	365	NP_006135	2431
HBA	NM_000558.3	34	366	NP_000549	2432
HBZ	NM_005332.2	35	367	NP_005323	2433
HBD	NM_000519.2	37	369	NP_000510	2434
HBE	NM_005330	38	370	NP_005321	2435
HBG	NM_000559.2	39	371	NP_000550	2436
HBQ	NM_005331	40	372	NP_005322	2437
HLA-DP	NM_033554	41	373	NP_291032	2438
HLA-DQ	NM_002122	42	374	NP_002113	2439
ICOS	NM_012092	44	376	NP_036224	2440
IL18	NM_001562	45	377	NP_001553	2441
IL3	NM_000588	46	378	NP_000579	2442
ITGA4	NM_000885	47	379	NP_000876	2443
ITGAM	NM_000632	48	380	NP_000623	2444
ITGB7	NM_000889	49	381	NP_000880	2445
CEBPB	NM_005194	50	382	NP_005185	2446
NF-E2	NM_006163	51	383	NP_006154	2447
PDCD1	NM_005018	52	384	NP_005009	2448
PF4	NM_002619	53	385	NP_002610	2449
PRKCQ	NM_006257.1	54	386	NP_006248	2450
PPARGC1	NM_013261	55	387	NP_037393	2451
RAG1	NM_000448	56	388	NP_000439	2452
RAG2	NM_000536	57	389	NP_000527	2453
CXCL12	NM_000609	58	390	NP_000600	2454
TNFRSF4	NM_003327	59	391	NP_003318	2455

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
TNFSF4	NM_003326	60	392	NP_003317	2456
TPS1	NM_003293	61	393	NP_003284	2457
ADA	NM_000022	62	394	NP_000013	2458
CPM	NM_001874.1	63	395	NP_001865	2459
CSF2	NM_000758.2	64	396	NP_000749	2460
CSF3	NM_172219	65	397	NP_757373	2461
CRP	NM_000567.1	66	398	NP_000558	2462
FLT3	NM_004119	67	399	NP_004110	2463
GATA3	NM_002051.1	68	400	NP_002042	2464
IL7R	NM_002185.1	69	401	NP_002176	2465
KLF1	NM_006563.1	70	402	NP_006554	2466
LCK	NM_005356.2	71	403	NP_005347	2467
LEF1	NM_016269.2	72	404	NP_057353	2468
PLAUR	NM_002659.1	73	405	NP_002650	2469
TNFSF13B	NM_006573.3	74	406	NP_006564	2470
IL8	NM_000584	75	407	NP_000575	2471
GZMB	NM_004131	76	408	NP_004122	2472
TNFSF6	NM_000639	77	409	NP_000630	2473
TCIRG1	NM_006019	78	410	NP_006010	2474
PRF1	NM_005041	79	411	NP_005032	2475
IL4	NM_000589	80	412	NP_000580	2476
IL13	NM_002188	81	413	NP_002179	2477
CTLA4	NM_005214	82	414	NP_005205	2478
CD8A	NM_001768	83	415	NP_001759	2479
BY55	NM_007053	84	416	NP_008984	2480
HBB	NM_000518	86	418	NP_000509	2481
BPGM	NM_001724	87	419	NP_001715	2482
MTHFD2	NM_006636	88	420	NP_006627	2483
TAP1	NM_000593	89	421	NP_000584	2484
OID_873	AK000354	94	426	NP_056212	2485
CXCR4	NM_003467	96	428	NP_003458	2486
CD69	NM_001781	97	429	NP_001772	2487
CCL5	NM_002985	98	430	NP_002976	2488
IL6	NM_000600	99	431	NP_000591	2489
IL2	NM_000586	100	432	NP_000577	2490
KLRF1	NM_016523	101	433	NP_057607	2491
LYN	NM_002350	102	434	NP_002341	2492
IL2RA	NM_000417	103	435	NP_000408	2493
CCL4	NM_002984	104	436	NP_002975	2494
ChGn	NM_018371	106	438	NP_060841	2495
CXCL9	NM_002416	108	440	NP_002407	2496
CXCL10	NM_001565	109	441	NP_001556	2497
IL17	NM_002190	110	442	NP_002181	2498
IL15	NM_000585	111	443	NP_000576	2499
IL10	NM_000572	112	444	NP_000563	2500
IFNG	NM_000619	113	445	NP_000610	2501
HLA-DRB1	NM_002124	114	446	NP_002115	2502
CD8B1	NM_004931	115	447	NP_004922	2503
CD4	NM_000616	116	448	NP_000607	2504
CXCR3	NM_001504	117	449	NP_001495	2505
CXCL1	NM_001511	120	452	NP_001502	2506
GPI	NM_000175	122	454	NP_000166	2507
CD47	NM_001777	123	455	NP_001768	2508
HLA-F	NM_018950	124	456	NP_061823	2509
PTGS2	NM_000963	128	460	NP_000954	2510
OID_5847	NM_144588	129	461	NP_653189	2511

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
PRDM1	NM_001198	130	462	NP_001189	2512
CKB	NM_001823	131	463	NP_001814	2513
TNNI3	NM_000363	132	464	NP_000354	2514
TNNT2	NM_000364	133	465	NP_000355	2515
MB	NM_005368	134	466	NP_005359	2516
SLC7A11	NM_014331	135	467	NP_055146	2517
TNFRSF5	NM_001250	136	468	NP_001241	2518
TNFRSF7	NM_001242	137	469	NP_001233	2519
CD86	NM_175862	138	470	NP_787058	2520
AIF1v2	NM_004847	139	471	NP_004838	2521
CMV IE1e3	NC_001347, compl	144	476	NP_040060	2522
CMV IE1e4	NC_001347, compl	145	477	NP_040060	2523
EV EBNA-1	NC_001345, 10795	146	478	NP_039875	2524
EV BZLF-1	NC_001345, compl	147	479	NP_039871	2525
CMV IE1	NC_001347, compl	150	482	NP_040060	2526
CMV IE1	NC_001347, compl	151	483	NP_040060	2527
CLC	NM_001828	152	484	NP_001819	2528
TERF2IP	NM_018975	153	485	NP_061848	2529
HLA-A	NM_002116	154	486	NP_002107	2530
MSCP	NM_018579	156	488	NP_061049	2531
DUSP5	NM_004419	157	489	NP_004410	2532
PRO1853	NM_018607	158	490	NP_061077	2533
CDSN	NM_001264	160	492	NP_001255	2534
RPS25	NM_001028	162	494	NP_001019	2535
GAPD	NM_002046	163	495	NP_002037	2536
RPLP1	NM_001003	164	496	NP_000994	2537
POLR2D	NM_004805	168	500	NP_004796	2538
ARPC3	NM_005719	169	501	NP_005710	2539
FPRL1	NM_001462	173	505	NP_001453	2540
FKBPL	NM_022110	174	506	NP_071393	2541
PREB	NM_013388	175	507	NP_037520	2542
OID_7595	NM_015653	177	509	NP_056468	2543
RNF19	NM_015435	178	510	NP_056250	2544
SMCY	NM_004653	179	511	NP_004644	2545
OID_7504	NM_152312	181	513	NP_689525	2546
DNAJC3	NM_006260	182	514	NP_006251	2547
ARHU	NM_021205	183	515	NP_067028	2548
OID_7200	NM_022752	184	516	NP_073589	2549
SERPINB2	NM_002575	185	517	NP_002566	2550
ENO1	NM_001428	186	518	NP_001419	2551
MOP3	NM_018183	193	525	NP_060653	2552
RPL18A	NM_000980	194	526	NP_000971	2553
INPP5A	NM_005539	195	527	NP_005530	2554
RPS29	NM_001032	197	529	NP_001023	2555
VNN2	NM_004665	200	532	NP_004656	2556
OID_7703	NM_014949	201	533	NP_055764	2557
EEF1A1	NM_001402	205	537	NP_001393	2558
PA2G4	NM_006191	206	538	NP_006182	2559
GAPD	NM_002046	207	539	NP_002037	2560
CHD4	NM_001273	208	540	NP_001264	2561
OID_7951	NM_016521	209	541	NP_057605	2562
DAB1	NM_021080	210	542	NP_066566	2563
OID_3406	NM_018986	211	543	NP_061859	2564
S100A8	NM_002964	215	547	NP_002955	2565
ERCC5	NM_000123	217	549	NP_000114	2566
RPS27	NM_001030	218	550	NP_001021	2567

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
ACRC	NM_052957	219	551	NP_443189	2568
UBL1	NM_003352	226	558	NP_003343	2569
SH3BGRL3	NM_031286	229	561	NP_112576	2570
SEMA7A	NM_003612	230	562	NP_003603	2571
IL21	NM_021803	233	565	NP_068575	2572
HERC3	NM_014606	234	566	NP_055421	2573
P11	NM_006025	236	568	NP_006016	2574
TIMM10	NM_012456	238	570	NP_036588	2575
EGLN1	AJ310543	239	571	NP_071334	2576
TBCC	NM_003192	240	572	NP_003183	2577
RNF3	NM_006315	241	573	NP_006306	2578
CCNDBP1	NM_012142	243	575	NP_036274	2579
SUV39H1	NM_003173	245	577	NP_003164	2580
HSPC048	NM_014148	246	578	NP_054867	2581
WARS	NM_004184	248	580	NP_004175	2582
SERPINB11	NM_080475	254	586	NP_536723	2583
RNF10	NM_014868	256	588	NP_055683	2584
MKRN1	NM_013446	257	589	NP_038474	2585
RPS16	NM_001020	258	590	NP_001011	2586
BAZ1A	NM_013448	259	591	NP_038476	2587
ATP5L	NM_006476	261	593	NP_006467	2588
NCBP2	NM_007362	264	596	NP_031388	2589
HZF12	NM_033204	266	598	NP_149981	2590
CCL3	D90144	267	599	NP_002974	2591
PRDX4	NM_006406	270	602	NP_006397	2592
BTK	NM_000061	271	603	NP_000052	2593
PGK1	NM_000291	273	605	NP_000282	2594
TNFRSF10A	NM_003844	274	606	NP_003835	2595
ADM	NM_001124	275	607	NP_001115	2596
C20orf6	NM_016649	277	609	NP_057733	2597
OID_3226	NM_015393	278	610	NP_056208	2598
ASAH1	NM_004315	279	611	NP_004306	2599
ATF5	NM_012068	280	612	NP_036200	2600
OID_4887	NM_032895	281	613	NP_116284	2601
MDM2	NM_002392	283	615	NP_002383	2602
XRN2	AF064257	284	616	NP_036387	2603
PRKRA	NM_003690	288	620	NP_003681	2604
CDKN1B	NM_004064	293	625	NP_004055	2605
PLOD	NM_000302	294	626	NP_000293	2606
FZD4	NM_012193	297	629	NP_036325	2607
HLA-B	NM_005514	298	630	NP_005505	2608
FPR1	NM_002029	300	632	NP_002020	2609
ODF2	NM_153437	301	633	NP_702915	2610
IL17C	NM_013278	307	639	NP_037410	2611
VPS45A	NM_007259	310	642	NP_009190	2612
HADHB	NM_000183	315	647	NP_000174	2613
FLJ22757	NM_024898	316	648	NP_079174	2614
NMES1	NM_032413	319	651	NP_115789	2615
DMBT1	NM_007329	320	652	NP_015568	2616
RPS23	NM_001025	321	653	NP_001016	2617
ZF	NM_021212	322	654	NP_067035	2618
NFE2L3	NM_004289	323	655	NP_004280	2619
RAD9	NM_004584	324	656	NP_004575	2620
DEFCAP	NM_014922	326	658	NP_055737	2621
IL22	NM_020525	328	660	NP_065386	2622
PSMA4	NM_002789	329	661	NP_002780	2623

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
CCNI	NM_006835	330	662	NP_006826	2624
THBD	NM_000361	331	663	NP_000352	2625
CGR19	NM_006568	332	664	NP_006559	2626
HSRRN18S	X03205	1	333		
HBB	NG_000007	36	368		
HLA-DRB		43	375		
OID_4460	AF150295	85	417		
KPNA6	AW021037	90	422		
OID_4365	AI114652	91	423		
IGHM	BC032249	92	424		
OID_573	AB040919	93	425		
OID_3	AW968823	95	427		
OID_6207	D20522	105	437		
OID_4281	AA053887	107	439		
OID_7094		118	450		
OID_7605	AA808018	119	451		
OID_253	AK091125	121	453		
OID_5350	AK055687	125	457		
TCRGC2	M17323	126	458		
OID_7016	BI018696	127	459		
EV EBV		141	473		
CMV p67	NC_001347	142	474		
CMV TRL7		143	475		
EV EBN		148	480		
EV EBNA-LP		149	481		
OID_5891	AW297949	155	487		
OID_6420	AK090404	159	491		
OID_4269	BM727677	161	493		
OID_5115	AI364926	165	497		
SLC9A8	AB023156	166	498		
OID_1512	BE618004	167	499		
OID_6282	BC041913	170	502		
PRO1073	AF001542	171	503		
OID_7222	BG260891	172	504		
OID_1551	BE887646	176	508		
OID_4184	X17403	180	512		
OID_7696	AW297325	187	519		
OID_4173	X17403	188	520		
CSF2RB	AL540399	189	521		
OID_7410	AW837717	190	522		
OID_4180	X17403	191	523		
OID_5101	BG461987	192	524		
hIAN7	BG772661	196	528		
OID_6008	AW592876	198	530		
OID_4186	X17403	199	531		
OID_7057	480F8	202	534		
OID_4291	BC038439	203	535		
OID_1366	AW850041	204	536		
OID_6986	AK093608	212	544		
OID_5962	AW452467	213	545		
OID_5152	AI392805	214	546		
HNRPU	BM467823	216	548		
PSMD11	AI684022	220	552		
OID_1016	AK024456	221	553		
OID_1309	AV706481	222	554		
OID_7582	AK027866	223	555		

Gene	ACC	SEQ ID 50mer	SEQ ID RNA/cDNA	RefSeq Peptide Accession #	SEQ ID Protein
OID_4317	AI318342	224	556		
OID_5889	AW297843	225	557		
OID_3687	W03955	227	559		
OID_7371	BE730505	228	560		
OID_5708	AW081540	231	563		
OID_5992	AW467992	232	564		
OID_7799	AW837717	235	567		
OID_7766	AW294711	237	569		
OID_6451	AL834168	242	574		
OID_8063	X68264	244	576		
OID_5625	AW063780	247	579		
OID_6823	AL832642	249	581		
OID_7073	AL705961	250	582		
OID_5339	AI625119	251	583		
OID_4263	AA136584	252	584		
MGC26766	AK025472	253	585		
OID_6711	BF968628	255	587		
OID_5998	AW468459	260	592		
OID_6393	52B9	262	594		
RoXaN	BC004857	263	595		
OID_6273	AW294774	265	597		
OID_4323	AA744774	268	600		
OID_5181	AI400725	269	601		
OID_6298	AI948513	272	604		
OID_357	138G5	276	608		
OID_4239	BQ022840	282	614		
OID_6039	BE502246	285	617		
OID_4210	AI300700	286	618		
OID_7698	AA243283	287	619		
OID_4288	AI378046	289	621		
OID_5620	AW063678	290	622		
OID_7384	BF475239	291	623		
OID_1209	C14379	292	624		
OID_5128	AK097845	295	627		
OID_5877	AW297664	296	628		
OID_5624	AW063921	299	631		
OID_5150	AI392793	302	634		
OID_5639	AW064243	303	635		
OID_6619	469A10	304	636		
OID_6933	AI089520	305	637		
OID_7049	480E2	306	638		
OID_5866	BM684739	308	640		
CD44	AA916990	309	641		
OID_4932	AA457757	311	643		
OID_7821	AA743221	312	644		
OID_4916	AA252909	313	645		
OID_4891	AL832329	314	646		
RAC1	AK054993	317	649		
OID_6415	CA407201	318	650		
OID_6295	AI880607	325	657		
RPL27A	BF214146	327	659		

Table 3: Viral genomes were used to design oligonucleotides for the microarrays. The accession numbers for the viral genomes used are given, along with the gene name and location of the region used for oligonucleotide design.

Virus	Gene Name	Genome Location
Adenovirus, type 2 Accession #J01917	E1a	1226..1542
	E1b_1	3270...3503
	E2a_2	complement(24089..25885)
	E3-1	27609..29792
	E4 (last exon at 3'-end)	complement(33193..32802)
	IX	3576..4034
	Iva2	complement(4081..5417)
	DNA Polymerase	complement(5187..5418)
Cytomegalovirus (CMV) Accession #X17403	HCMVTRL2 (IRL2)	1893..2240
	HCMVTRL7 (IRL7)	complement(6595..6843)
	HCMVUL21	complement(26497..27024)
	HCMVUL27	complement(32831..34657)
	HCMVUL33	43251..44423
	HCMVUL54	complement(76903..80631)
	HCMVUL75	complement(107901..110132)
	HCMVUL83	complement(119352..121037)
	HCMVUL106	complement(154947..155324)
	HCMVUL109	complement(157514..157810)
	HCMVUL113	161503..162800
	HCMVUL122	complement(169364..170599)
	HCMVUL123 (last exon at 3'-end)	complement(171006..172225)
	HCMVUS28	219200..220171
Epstein-Barr virus (EBV) Accession # NC_001345	Exon in EBNA-1 RNA	67477..67649
	Exon in EBNA-1 RNA	98364..98730
	BRLF1	complement(103366..105183)
	BZLF1 (first of 3 exons)	complement(102655..103155)
	BMLF1	complement(82743..84059)
	BALF2	complement(161384..164770)
Human Herpesvirus 6 (HHV6) Accession #NC_001664	U16/U17	complement(26259..27349)
	U89	complement(133091..135610)
	U90	complement(135664..135948)
	U86	complement(125989..128136)
	U83	123528..123821
	U22	complement(33739..34347)
	DR2 (DR2L)	791..2653
	DR7 (DR7L)	5629..6720
	U95	142941..146306
	U94	complement(141394..142866)
	U39	complement(59588..62080)
	U42	complement(69054..70598)
	U81	complement(121810..122577)
	U91	136485..136829

Table 4: Dependent variables for discovery of gene expression markers of cardiac allograft rejection.

Dependent Variable	Description	Number of Rejection Samples	Number of No-Rejection Samples
0 vs 1-4 Bx	Grade 0 vs. Grades 1-4, local biopsy reading	65	114
s0 vs 1B-4 HG	Stable Grade 0 vs Grades 1B-4, highest grade, Grade 1A not included	41	57
0-1A vs 1B-4 HG	Grades 0 and 1A vs Grades 1B-4, highest grade.	121	58
0 vs 3A HG	Grade 0 vs Grade 3A, highest grade. Grades 1A-2 and Grade 3B were not included.	56	29
0 vs 1B-4	Grade 0 vs Grades 1B-4, highest grade. Grade 1A was not included.	57	57
0 vs 1A-4	Grade 0 vs. Grades 1-4, highest grade	56	123

Table 5: Real-time PCR assay chemistries. Various combinations of reporter and quencher dyes are useful for real-time PCR assays.

Reporter	Quencher
FAM	TAMRA
	BHQ1
TET	TAMRA
	BHQ1
JOE	TAMRA
	BHQ1
HEX	TAMRA
	BHQ1
VIC	TAMRA
	BHQ1
ROX	BHQ2
TAMRA	BHQ2

Table 6: Real-time PCR results for rejection markers

Gene Array Probe SEQ ID	Phase 1				Phase 2				All Data			
	Fold	t-Test	NR	R	Fold	t-Test	NR	R	Fold	t-Test	NR	R
95	1.093	0.36084	10	8					0.935	0.31648	21	13
111	1.415	0.0095	12	10					1.415	0.0095	12	10
79	1.822	0.01146	6	7	0.63	0.04185	19	15	0.72	0.05632	35	26
3016	1.045	0.41017	12	10					1.001	0.49647	16	15
75	0.84	0.36674	11	8	0.595	0.15788	16	13	0.628	0.08402	34	26
2765	1.653	0.01508	10	10	0.776	0.11082	19	14	0.956	0.37421	38	29
97					0.75	0.26201	8	8	0.543	0.11489	17	12
2635	1.553	0.00533	13	10	0.834	0.16853	18	15	0.988	0.46191	36	27
96	1.495	0.06288	13	9	1.157	0.27601	18	15	1.155	0.21096	33	25
100	1.43	0.166	10	5					1.408	0.14418	12	8
2766	0.956	0.43918	12	10	0.989	0.48275	19	14	0.978	0.45101	31	24
2726	1.037	0.38205	11	9					1.037	0.38205	11	9
2768	1.211	0.02386	9	9					1.211	0.02386	9	9
94	1.601	0.02418	11	10					1.831	0.00094	17	15
2769	1.133	0.23094	12	9	1.081	0.19632	19	15	1.101	0.15032	31	24
2770	1.734	0.00017	13	10					1.381	0.01323	20	15
2647	1.557	0.04502	10	8					1.557	0.04502	10	8
2771	1.99	0.05574	13	9					1.52	0.11108	17	13
82	2.029	0.00022	8	5	1.287	0.13022	18	14	1.256	0.05356	33	23
83	1.546	0.05865	13	10	0.577	0.03934	18	14	0.795	0.11993	39	26
98					0.716	0.13	19	15	0.577	0.03352	19	14
36	1.605	0.09781	12	8	2.618	0.01227	18	11	2.808	0.00015	38	23
80	5.395	0.00049	9	6	4.404	0.05464	10	10	2.33	0.02369	29	18
89									0.295	0.02856	6	6
77	1.894	0.01602	10	10	0.537	0.01516	19	15	0.863	0.21987	35	29
2772	1.583	0.06276	10	6	0.714	0.13019	13	10	1.136	0.28841	28	17
2773	1.391	0.09236	11	6					1.391	0.09236	11	6
2774	1.59	0.00022	13	10					1.59	0.00022	13	10
102	1.245	0.05079	11	10	1.018	0.42702	17	15	1.117	0.08232	32	28
2775	0.719	0.16243	11	9					0.719	0.16243	11	9
2776	1.257	0.0516	12	9					1.257	0.0516	12	9
2667	1.343	0.03806	13	9					1.13	0.15962	20	12
115	1.199	0.26299	11	9					1.199	0.26299	11	9
2669	2.146	0.00813	12	10					1.296	0.14285	18	12
2777	1.142	0.20245	13	10					1.142	0.20245	13	10
78	1.324	0.01985	12	9	0.967	0.33851	18	14	1.007	0.46864	38	24
2670	1.388	0.11209	13	9					1.388	0.11209	13	9
88	1.282	0.14267	7	7	0.995	0.48504	17	14	1.008	0.47383	30	23
2778	1.128	0.19528	13	9					1.128	0.19528	13	9
2779	1.991	0.02513	9	5	0.642	0.05002	18	14	0.868	0.26275	32	21
2780	1.597	0.00355	13	10	0.802	0.11649	17	14	1.013	0.45521	38	26
2781					0.492	0.01344	12	12	0.819	0.25555	17	15

Table 6: Real-time PCR results for rejection markers

Gene Array Probe SEQ ID	Phase 1				Phase 2				All Data			
	Fold	t-Test	NR	R	Fold	t-Test	NR	R	Fold	t-Test	NR	R
101					0.652	0.04317	19	15	0.773	0.09274	29	22
106	1.234	0.19141	13	8					1.234	0.19141	13	8
2683	1.598	0.03723	8	8	0.633	0.03893	14	10	0.86	0.18731	28	22
2782	1.213	0.03305	12	10	0.912	0.07465	19	15	0.969	0.31955	39	27
87					4.947	0.02192	18	15	3.857	0.00389	30	23
99	0.639	0.06613	7	5	0.839	0.30304	16	8	0.694	0.04347	27	15
2692	0.801	0.21236	12	8	0.893	0.33801	18	15	0.782	0.06938	38	25
104	2.292	0.0024	11	8	0.621	0.05152	19	15	0.913	0.34506	30	23
76	1.809	0.00893	9	8	0.693	0.13027	13	8	1.274	0.11887	28	19
91	1.969	0.07789	11	8	4.047	0.00812	19	13	3.535	0.00033	37	23
92	2.859	0.05985	11	8	9.783	0.03047	18	14	8.588	0.00192	37	24
85	0.95	0.43363	12	8	0.699	0.0787	13	13	0.633	0.01486	33	24
126	1.76	0.02199	11	10					1.76	0.02199	11	10
2783	0.945	0.46023	10	5	0.852	0.26701	17	10	0.986	0.48609	29	17
2707	1.055	0.31435	13	10					1.055	0.31435	13	10
123	1.154	0.11677	11	10					1.154	0.11677	11	10
84	1.786	0.00255	9	6	0.523	0.04965	18	14	0.785	0.14976	34	22
2784	2.12	0.00022	12	10	0.498	0.01324	18	13	0.935	0.37356	37	25
2785	1.181	0.1377	10	10					1.181	0.1377	10	10
124	1.353	0.08122	11	9					1.353	0.08122	11	9
90	1.355	0.02288	13	10	0.973	0.39248	15	13	1.125	0.08671	28	23
2786	1.306	0.0773	12	10					1.306	0.0773	12	10
2787	1.086	0.32378	12	10					1.086	0.32378	12	10
3018	1.523	0.1487	12	10	0.84	0.27108	18	13	1.101	0.33276	36	26
125	1.252	0.05782	11	10					1.252	0.05782	11	10
2788	1.255	0.1221	11	10					1.255	0.1221	11	10
2789	1.152	0.31252	9	6					1.152	0.31252	9	6
3019	1.268	0.21268	6	7	0.981	0.45897	16	10	1.012	0.46612	29	19
2790	0.881	0.17766	11	8	1.22	0.04253	18	10	0.966	0.33826	40	23
2791	1.837	0.00553	13	10					1.837	0.00553	13	10
3020	1.271	0.10162	12	10	0.853	0.10567	19	13	0.965	0.36499	36	25
2792	1.504	0.05096	12	10	0.713	0.02979	19	15	0.846	0.16914	31	25
2793	1.335	0.03133	12	10	0.883	0.18577	19	15	0.916	0.23865	36	27
2794	1.936	0.00176	13	9	0.717	0.09799	19	14	0.877	0.22295	40	25
2752	1.499	0.03077	12	8	0.808	0.15363	17	13	1.004	0.48903	36	23
2795	0.815	0.24734	8	5	0.965	0.41772	19	15	0.938	0.3265	32	22
119	1.272	0.20279	10	10					1.272	0.20279	10	10

Table 7: Significance analysis for microarrays for identification of markers of acute rejection. In each case the highest grade from the 3 pathologists was taken for analysis. No rejection and rejection classes are defined. Samples are either used regardless of redundancy with respect to patients or a requirement is made that only one sample is used per patient or per patient per class. The number of samples used in the analysis is given and the lowest FDR achieved is noted.

No Rejection	Rejection	# Samples	Low FDR
All Samples			
Grade 0	Grade 3A-4	148	1
Grade 0	Grade 1B, 3A-4	158	1.5
Non-redundant within class			
Grade 0	Grade 3A-4	86	7
Grade 0	Grade 1B, 3A-4	93	16
Non-redundant (1 sample/patient)			
Grade 0	Grade 3A-4	73	11

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2697	CD69 antigen (p60, early T-cell activat	1.5625	2925	+	
2645	Ras association (RalGDS/AF-6)	1.5625	2926		
2707	CD33 antigen (gp67) (CD33), mRNA	1.5625	2927	+	
2679	Ras association (RalGDS/AF-6) domain fa	1.5625	2928		
2717	EST, 5 end	1.5625			
2646	mRNA for KIAA0209 gene, partial cds /cd	1.5625	2929		
2667	leupaxin (LPXN), mRNA /cds=(93,1253)	1.5625	2930	+	
2706	c- EST 3 end /clone=IMAGE:	2.1111			
2740	c- insulin induced gene 1 (INSIG1), mRNA	2.2			
117	chemokine (C-X-C motif) receptor 3	2.8125	2931		
2669	IL2-inducible T-cell kinase (ITK), mRNA	2.8125	2932	+	
2674	glioma pathogenesis-related protein (RT	2.8125	2933		
2743	c- nuclear receptor subfamily 1, group I	2.8125			
326	death effector filament-forming Ced-4-I	2.8125	2934		
2716	EST cDNA, 3 end	2.8125			
2727	c- chemokine (C-X-C motif), receptor 4	3.1316	2935	+	
2721	c- EST 3 end /clone=IMAGE:	3.1316			
2641	hypothetical protein FLJ20647 (FLJ20647	3.1316	2936		
2671	tumor necrosis factor, alpha-induced pr	3.525	2937		
2752	protein tyrosine phosphatase, receptor	3.8077	2938	+	
2737	7f37g03.x1 cDNA, 3 end /clone=IMAGE:	3.8077			
2719	c- EST372075 cDNA	3.8077			
2684	molecule possessing ankyrin repeats ind	3.8077	2939		
76	granzyme B (granzyme 2, cytotoxic T-lym	3.8077	2940	+	+
2677	lectin-like NK cell receptor (LLT1), mR	3.8077	2941	+	
2748	c-107G11	3.9			
2703	c- EST, 5 end /clone=IMAGE	3.9			
2711	SAM domain, SH3 domain and nuclear	3.9	2942		
2663	phosphodiesterase 4B, cAMP-specific	3.9	2943		+
98	small inducible cytokine A5 (RANTES)	4.5645	2944	+	+
2657	tumor necrosis factor receptor superfam	4.8286	2945		
2683	B-cell lymphoma/leukaemia 11B (BCL11B)	4.8286	2946	+	
2686	phospholipase A2, group VII (platelet-a	4.8286	2947		+
2687	phosphatidylinositol 3-kinase catalytic	4.8286	2948		
2644	AV659177 cDNA, 3 end	4.9028			
2664	regulator of G-protein signalling 10 (R	5.0238	2949		
2747	c- integral membrane protein 2A (ITM2A),	5.0238	2950		
2744	c- interferon consensus sequence binding	5.0238			
2678	HSPC022 protein (HSPC022), mRNA	5.0238	2951		
2731	c- xj98c03.x1 NCI_CGAP_Co18 cDNA	5.0238			
2713	caspase recruitment domain protein 9 (L	5.0238	2952		
2736	c- small inducible cytokine A4 (homologo	5.1395	2953	+	+
2708	major histocompatibility complex, class	5.15	2954		
249	c-107H8	5.15			
2670	CD72 antigen (CD72), mRNA	5.15	2955	+	
2661	heat shock 70kD protein 6 (HSP70B)	5.15	2956		
2680	bridging integrator 2 (BIN2), mRNA /cds	5.15	2957		
2754	UI-H-BW0-aiy-b-10-0-UI.s1 cDNA, 3 end	5.15			
2728	c- EST380762 cDNA	5.15			
174	FKBPL	5.15	2958		
2742	c- chromobox homolog 3 (DM)	5.15			
2668	basement membrane-induced gene(ICB-1)	5.15	2959		
2750	Lysosomal-assoc. multispanning memb	5.15	2960		

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2746	174D1	5.15			
2738	c- AV716627 cDNA, 5 end	5.15			
2627	solute carrier family 17 (sodium phosph	5.15	2961		
2739	c- asparaginyl-tRNA synthetase (NARS)	5.15			
124	major histocompatibility complex, class	5.15	2962		
2647	mRNA for T-cell specific protein /cds	5.15	2963	+	
2628	c-EST, 3 end	5.2295			
2638	Express cDNA library cDNA 5	5.2903			
2725	c- 601571679F1 cDNA, 5 end	5.3385	2964		
2714	qg78c05.x1 cDNA, 3 end /clone	5.3385	2965		
2635	interleukin 2 receptor gamma chain	5.3385	2966	+	
2751	7264, lectin, galactoside-binding, soluble	5.4167	2967		+
2629	8, cDNA: FLJ21559 fis, clone COL06406	5.5299	2968		
2695	mRNA; cDNA DKFZp434E0516	5.5588	2969		
2741	c- hexokinase 2 (HK2), mRNA	5.5986			
41	Similar to major histocompatibility antigen	5.5986	2970		
2691	CD5 antigen (p56-62) (CD5)	5.5986	2971		
2726	c- 602650370T1 cDNA, 3	5.6014			
2722	c- EST cDNA clone	5.6014			
2689	interleukin-2 receptor	5.6014	2972		
2734	c- nuclear receptor subfamily 1, group I	5.6667			
2631	pre-B-cell colony-enhancing factor	5.7566	2973		+
2656	postmeiotic segregation increased	5.7756	2974		
2696	protein tyrosine phosphatase, receptor	5.7756	2975	.	
2676	butyrophilin, subfamily 3, member A2	5.8165	2976		
2701	c- EST 3 end	5.9048			
2730	EST 3 end /clone=IMAGE	5.9048			
2710	high affin. immunoglobulin epsilon recept.	5.9048	2977		
2632	encoding major histocompatibility comple	5.9048	2978		
2724	c- EST 3 end	5.9048			
2698	EST	6.0353			
2662	interferon regulatory factor 1 (IRF1),	6.0988	2979		
139	allograft inflammatory factor 1 (AIF1),	6.1379	2980		
2753	platelet activating receptor homolog (H ·	6.3182	2981		
2704	c- EST 3 end /clone=IMAGE:	7.0337			
2675	pim-2 oncogene (PIM2), mRNA	7.1222	2982		+
2700	proteoglycan 1, secretory granule (PRG1	7.375	2983		+
2640	mRNA for KIAA0870 protein, partial cds	7.375	2984		
2723	c- EST, 5 end /clone=IMAGE	7.375			
2658	FYN-binding protein (FYB-120/130) (FYB)	7.375	2985		
2688	major histocompatibility complex, class	7.375	2986		
2735	c- EST, 3 end /clone=IMAGE:	7.375			
2702	c- hypothetical protein MGC4707	7.634			
2681	hypothetical protein FLJ10652	8.1117	2987		
2755	EST, 3 end	8.1117			
2715	hypothetical protein FLJ10842	8.1117			
2732	c- EST cDNA, 3 end	8.1117			
2652	hexokinase 2 (HK2), mRNA	8.1117			
2651	colony stimulating factor 3 receptor	8.1117	2988		
2718	RNA binding motif protein, X chrom	8.2788			
2673	Src-like-adapter (SLA), mRNA	8.3048	2989		
2733	c- major histocompatibility complex	8.467			
2712	histamine receptor H2 (HRH2)	8.8583	2990		

Table 8: Renal rejection tissue gene expression SAM analysis

Array probe ID	Gene	FDR	Protein SEQ ID	Leukocyte expression	Secreted
2659	hemopoietic cell kinase (HCK)	8.8583	2991		
2654	xanthene dehydrogenase (XDH)	8.8583	2992		
2636	Arabidopsis root cap 1	8.8583	2993		
2639	fatty acid binding protein 1, liver	8.8583			
2690	adenosine deaminase (ADA)	8.8583	2994		
2705	c- EST, 3 end	8.8583	2995		
2685	hypothetical protein MGC10823	8.8583	2996		
2692	membrane-spanning 4-domains,	8.8583	2997		
2693	rearranged immunoglobulin mRNA for mu	8.8583			+
2648	protein tyrosine kinase related mRNA	8.8583			
2650	major histocompatibility complex, class	8.8583	2998		
2720	c- EST 3 end /clone=IMAGE:	8.8583			
2660	major histocompatibility complex, class	8.8583	2999		
2666	BCL2-related protein A1 (BCL2A1), mRNA	9.1446	3000		
2699	c-EST	9.4767			
2633	interleukin 4 receptor	9.4767	3001		
74	tumor necrosis factor (ligand) superfam	9.4767	3002		
2672	interferon-induced, hepatitis C-assoc.	9.4767	3003		
2642	cDNA FLJ20673 fis, clone KAIA4464	9.4767	3004		
2682	VNN3 protein (HSA238982), mRNA	9.4767	3005		
2655	cathepsin K (pycnodysostosis) (CTSK)	9.4767	3006		
2630	Integrin, alpha L (CD11A (p180), lymphoc	9.4767	3007		
2745	EST, 5 end	9.4885	3008		
2643	nuclear receptor subfamily 1, group I,	9.625			
2694	CDW52 antigen (CAMPATH-1)	9.625	3009		
2749	6977, c-178F5	9.6903	3010		
2665	small inducible cytokine subfamily A	9.6903	3011		
2649	signal transducer and activator	9.7878	3012		
2637	324,	9.7878			
2634	70 activation (Act-2) mRNA	9.7878	3013		
2709	coagulation factor VII	9.7878	3014		
2653	integrin, beta 2 (antigen CD18 (p95)	9.7878	3015		
2729	EST 3' end	9.8321			

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
111	IL15	Interleukin 15	NM_000585	NP_000576	Hs.168132	Secreted	T-cell activation and proliferation
79	PRF1	Perforin 1 (pore forming protein)	NM_005041	NP_005032	Hs.2200	Secreted	CD8, CTL effector; channel-forming protein capable of lysing non-specifically a variety of target cells; clearance of virally infected host cells and tumor cells; .
110	IL17	Interleukin 17 (cytotoxic T-lymphocyte-associated serine esterase 8)	NM_002190	NP_002181	Hs.41724	Secreted	Induces stromal cells to produce proinflammatory and hematopoietic cytokines; enhances IL6, IL8 and ICAM-1 expression in fibroblasts; osteoclastic bone resorption in RA; expressed in only in activated CD4+T cells
75	IL8	Interleukin 8	NM_000584	NP_000575	Hs.624	Secreted	Proinflammatory cytokine
120	CXCL1	Chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	NM_001511	NP_001502	Hs.789	Secreted	Neurogenesis, immune system development, signaling
113	IFNG	Interferon, gamma	NM_000619	NP_000610	Hs.856	Secreted	Antiviral defense and immune activation
100	IL2	Interleukin 2	NM_000586	NP_000577	Hs.89679	Secreted	Promotes growth of B and T cells
4	B2M	beta 2 microglobulin	NM_004048	NP_004039	Hs.75415	Secreted	
98	CCL5	Chemokine (C-C motif) ligand 5 (RANTES, SCYA5)	NM_002985	NP_002976	Hs.241392	Secreted	Chemoattractant for monocytes, memory T helper cells and eosinophils; causes release of histamine from basophils and activates eosinophils; One of the major HIV-suppressive factors produced by CD8+ cells
112	IL10	Interleukin 10	NM_000572	NP_000563	Hs.193717	Secreted	Chemotactic factor for CD8+T cells; down-regulates expression of Th1 cytokines, MHC class II Ags, and costimulatory molecules on macrophages; enhances B cell survival, proliferation, and antibody production; blocks NF kappa B, JAK-STAT regulation;
80	IL4	Interleukin 4	NM_000589	NP_000580	Hs.73917	Secreted	TH2, cytokine, stimulates CTL
2773	IL7	Interleukin 7	NM_000880	NP_000871	Hs.72927	Secreted	Proliferation of lymphoid progenitors

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
109	CXCL10	Chemokine (C-X-C motif) ligand 10, SCYB10	NM_001565	NP_001556	Hs.2248	Secreted	Stimulation of monocytes; NK and T cell migration, modulation of adhesion molecule expression
2665	CCL17	Chemokine (C-C motif) ligand 17	NM_002987	NP_002978	Hs.66742	Secreted	T cell development, trafficking and activation
101	KLRF1	Killer cell lectin-like receptor subfamily F, member 1	NM_016523	NP_057607	Hs.183125	Secreted	Induction of IgE, IgG4, CD23, CD72, surface IgM, and class II MHC antigen in B cells
99	IL6	Interleukin 6	NM_000600	NP_000591	Hs.93913	Secreted	B cell maturation
104	CCL4	Chemokine (C-C motif) ligand 4	NM_002984	NP_002975	Hs.75703	Secreted	Inflammatory and chemokinetic properties; one of the major HIV-suppressive factors produced by CD8+ T cells
76	GZMB	Granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	NM_004131	NP_004122	Hs.1051	Secreted	Apoptosis; CD8, CTL effector
2785	OID_4789	KIAA0963 protein	NM_014963	NP_055778	Hs.7724	Secreted	Proinflammatory; chemoattraction and activation of neutrophils
2791	XCL1	Chemokine (C motif) ligand 1 (SCYC2)	NM_002995	NP_002986	Hs.3195	Secreted	Chemotactic factor for lymphocytes but not monocytes or neutrophils
130	PRDM1	PR domain containing 1, with ZNF domain	NM_001198	NP_001189	Hs.388346	Nuclear	Transcription factor; promotes B cell maturation, represses human beta-IFN gene expression
2781	TBX21	T-box 21	NM_013351	NP_037483	Hs.272409	Nuclear	TH1 differentiation, transcription factor
88	MTHFD2	Methylene tetrahydrofolate dehydrogenase (NAD+ dependent), methenyltetrahydrofolate cyclohydrolase	NM_006636	NP_006627	Hs.154672	Mitochondrial	Folate metabolism
103	IL2RA	Interleukin 2 receptor, alpha	NM_000417	NP_000408	Hs.1724	Membrane-bound and soluble forms	T cell mediated immune response
77	TNFSF6	Tumor necrosis factor (ligand) superfamily, member 6	NM_000639	NP_000630	Hs.2007	Membrane-bound and soluble forms	CD8, CTL effector; proapoptotic
115	CD8B1	CD8 antigen, beta polypeptide 1 (p37)	NM_004931	NP_004922	Hs.2299	Membrane-bound and soluble forms	CTL mediated killing
128	PTGS2	Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	NM_000963	NP_000954	Hs.196384	Membrane-associated	Angiogenesis, cell migration, synthesis of inflammatory prostaglandins

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
89	TAP1	Transporter 1, ATP-binding cassette, sub-family B (MDR1/TAP)	NM_000593	NP_000584	Hs.352018	ER membrane	Transports antigens into ER for association with MHC class I molecules
92	IGHM	Immunoglobulin heavy constant mu	BC032249		Hs.300697	Cytoplasmic and secreted forms	Antibody subunit
122	GPI	Glucose phosphate isomerase	NM_000175	NP_000166	Hs.409162	Cytoplasmic and secreted forms	Glycolysis and gluconeogenesis (cytoplasmic); neurotrophic factor (secreted)
2783	GSN	Gelsolin (amyloidosis, Finnish type)	NM_000177	NP_000168	Hs.290070	Cytoplasmic and secreted forms	Controls actin filament assembly/disassembly
2780	STK39	Serine threonine kinase 39 (STE20/SPS1 homolog, yeast)	NM_013233	NP_037365	Hs.199263	Cytoplasmic and nuclear	Mediator of stress-activated signals; Serine/Thr Kinase, activated p38
2770	PSMB8	Proteasome (prosome, macropain) subunit, beta type, 8 (large multifunctional protease 7)	AK092738		Hs.180062	Cytoplasmic	Processing of MHC class I antigens
2667	LPXN	Leupaxin	NM_004811	NP_004802	Hs.49587	Cytoplasmic	Signal transduction
2669	ITK	IL2-inducible T-cell kinase	L10717		Hs.211576	Cytoplasmic	Intracellular kinase, T-cell proliferation and differentiation
90	KPNA6	Karyopherin alpha 6 (importin alpha 7)	AW021037		Hs.301553	Cytoplasmic	Nucleocytoplasmic transport
2794	SH2D2A	SH2 domain protein 2A	NM_003975	NP_003966	Hs.103527	Cytoplasmic	CD8 T activation, signal transduction
2765	TNFSF5	Tumor necrosis factor (ligand) superfamily, member 5 (hyper-IgM syndrome)	NM_000074	NP_000065	Hs.652	Cellular membrane	B-cell proliferation, IgE production, immunoglobulin class switching; expressed on CD4+ and CD8+ T cells
97	CD69	CD69 antigen (p60, early T-cell activation antigen)	NM_001781	NP_001772	Hs.82401	Cellular membrane	Activation of lymphocytes, monocytes, and platelets
2635	IL2RG	Interleukin 2 receptor, gamma (severe combined immunodeficiency)	NM_000206	NP_000197	Hs.84	Cellular membrane	Signalling component of many interleukin receptors (IL2,IL4,IL7,IL9, and IL15),
96	CXCR4	Chemokine (C-X-C motif) receptor 4	NM_003467	NP_003458	Hs.89414	Cellular membrane	B-cell lymphopoiesis, leukocyte migration, angiogenesis; mediates intracellular calcium flux
2766	CD19	CD19 antigen	NM_001770	NP_001761	Hs.96023	Cellular membrane	Signal transduction; B lymphocyte development, activation, and differentiation

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
2769	ITGB1	Integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	NM_002211	NP_002202	Hs.287797	Cellular membrane	Cell-cell and cell-matrix interactions
2647	TRB	T cell receptor beta, constant region	K02885		Hs.300697	Cellular membrane	Antigen recognition
82	CTLA4	Cytotoxic T-lymphocyte-associated protein 4	NM_005214	NP_005205	Hs.247824	Cellular membrane	Negative regulation of T cell activation, expressed by activated T cells
83	CD8A	CD8 antigen, alpha polypeptide (p32)	NM_001768	NP_001759	Hs.85258	Cellular membrane	CD8 T-cell specific marker and class I MHC receptor
114	HLA-DRB1	Major histocompatibility complex, class II, DR beta 1	NM_002124	NP_002115	Hs.308026	Cellular membrane	Antigen presentation
2772	CD3Z	CD3Z antigen, zeta polypeptide (TiT3 complex)	NM_000734	NP_000725	Hs.97087	Cellular membrane	T-cell marker; couples antigen recognition to several intracellular signal-transduction pathways
2	ACTB	Actin, beta	NM_001101	NP_001092	Hs.288061	Cellular membrane	Cell adhesion and recognition
2774	ITGAL	Integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	NM_002209	NP_002200	Hs.174103	Cellular membrane	All leukocytes; cell-cell adhesion, signaling
78	TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 protein a isoform 3	NM_006019	NP_006010	Hs.46465	Cellular membrane	T cell activation.
2670	CD72	CD72 antigen	NM_001782	NP_001773	Hs.116481	Cellular membrane	B cell proliferation
2779	D12S2489E	DNA segment on chromosome 12 (unique) 2489 expressed sequence	NM_007360	NP_031386	Hs.74085	Cellular membrane	NK cells marker
2692	MS4A1	Membrane-spanning 4-domains, subfamily A, member 1, CD20	NM_152866	NP_690605	Hs.89751	Cellular membrane	B-cell activation, plasma cell development
126	TCRGC2	T cell receptor gamma constant 2	M17323		Hs.112259	Cellular membrane	
116	CD4	CD4 antigen (p55)	NM_000616	NP_000607	Hs.17483	Cellular membrane	T cell activation, signal transduction, T-B cell adhesion

Table 9

Array Probe SEQ ID	Gene	Gene Name	mRNA Accession #	RefSeq Peptide Accession #	Current UniGene Cluster (Build 156)	Localization	Function
117	CXCR3	Chemokine (C-X-C motif) receptor 3, GPR9	NM_001504	NP_001495	Hs.198252	Cellular membrane	Integrin activation, cytoskeletal changes and chemotactic migration of leukocytes
2707	CD33	CD33 antigen (gp67)	NM_001772	NP_001763	Hs.83731	Cellular membrane	Cell adhesion; receptor that inhibits the proliferation of normal and leukemic myeloid cells
123	CD47	CD47 antigen (Rh-related antigen, integrin-associated signal transducer)	NM_001777	NP_001768	Hs.82685	Cellular membrane	Cell adhesion, membrane transport, signaling transduction, permeability
84	BY55	Natural killer cell receptor, immunoglobulin superfamily member	NM_007053	NP_008984	Hs.81743	Cellular membrane	NK cells and CTLs, costim with MHC I
2784	KLRD1	Killer cell lectin-like receptor subfamily D, member 1	NM_002262	NP_002253	Hs.41682	Cellular membrane	NK cell regulation
124	HLA-F	Major histocompatibility complex, class I, F	NM_018950	NP_061823	Hs.377850	Cellular membrane	Antigen presentation
2752	PTPRCAP	Protein tyrosine phosphatase, receptor type, C-associated protein	NM_005608	NP_005599	Hs.155975	Cellular membrane	T cell activation

Table 12: Markers for CMV Infection

New SEQID	Source	Unigene	Acc	GI	Name	Strand	Probe Sequence	SAM FDR
408	cDNA	Hs.1051	NM_004131	7262379	granzyme B	1	GGAGCCAAGTCCAGATT TACACTGGGAGAGGTGC CAGCAACTGAATAAAT	0%
3108	db mining	Hs.169824	NM_002258	4504878	killer cell lectin-like receptor	1	TGGATCTGCCAAAAAGA ACTAACACCTGTGAGAA ATAAAGTGTATCCTGA	0%
3109	cDNA	Hs.170019	NM_004350	4757917	runt-related transcription factor 3	1	GCTGGGTGGAAACTGCT TTGCACTATCGTTTGCT TGGTGTTTGTTTTTAA	0%
433	cDNA	Hs.183125	NM_016523	7705573	killer cell lectin-like receptor F	1	TTCCAGGCTTTTGCTAC TCTTCACTCAGCTACAA TAAACATCCTGAATGT	0%
3110	db mining	Hs.2014	X06557	37003	T-cell receptor-delta	1	GGGGTTTATGTCCTAAC TGCTTTGTATGCTGTTT TATAAAGGGATAGAAG	0.10%
3111	cDNA	Hs.211535	AI823649	5444320	EST IMAGE:240014 8	-1	GAAGCCTTTTCTTTTCT GTTCACCCTCACCAAGA GCACAACTTAAATAGG	0.10%
3112	cDNA	Hs.301704	AW002985	5849991	eomesodermin (Xenopus laevis)	-1	AACAAGCCATGTTTGCC CTAGTCCAGGATTGCCT CACTTGAGACTTGCTA	0%
3112	Table 3B	Hs.301704	AW002985	5849991	eomesodermin (Xenopus laevis)	-1	AACAAGCCATGTTTGCC CTAGTCCAGGATTGCCT CACTTGAGACTTGCTA	0%
3113	cDNA	Hs.318885	NM_000636	10835186	superoxide dismutase 2	1	TACTTTGGGGACTTGTA GGGATGCCTTTCTAGTC CTATTCTATTGCAGTT	0.10%
3114	literature	Hs.41682	NM_007334	7669498	killer cell lectin-like receptor D	1	GGGCAGAGAAGGTGGAG AGTAAAGACCCAACATT ACTAACAATGATACAG	0%
3115	cDNA	Hs.71245	AI954499	5746809	EST IMAGE:502221	-1	TGGTAATAGTGTTTGAC TCCAGGGAAGAACAGAT GGGGTGCCAGAGTGAAA	0%
3116	cDNA	Hs.75596	NM_000878	4504664	interleukin 2 receptor, beta	1	ATGGAAATTGTATTTGC CTTCTCCACTTTGGGAG GCTCCCACTTCTTGGG	0%
436	cDNA	Hs.75703	NM_002984	4506844	small inducible cytokine A4	1	CCACTGTCACTGTTTCT CTGCTGTTGCAAATACA TGGATAACACATTTGA	0%
436	cDNA	Hs.75703	NM_002984	4506844	small inducible cytokine A4	1	CCACTGTCACTGTTTCT CTGCTGTTGCAAATACA TGGATAACACATTTGA	0.10%
436	cDNA	Hs.75703	NM_002984	4506844	small inducible cytokine A4	1	GTCCACTGTCACTGTTT CTCTGCTGTTGCAAATA CATGGATAACACATTT	0%
436	cDNA	Hs.75703	NM_002984	4506844	small inducible cytokine A4	-1	TGGTCCACTGTCACTGT TTCTCTGCTGTTGCAAA TACATGGATAACACAT	0.10%
415	cDNA	Hs.85258	BC025715	19344021	CD8 antigen	1	CTGAGAGCCCAAACTGC TGTCCCAAACATGCACT TCCTTGCTTAAGGTAT	0.10%
3117	cDNA	Hs.111554	AA806222	2874972	cDNA 196D7	-1	TGATTTCTGTAATGTTT GACCTAATAATAGCCCT TTTCGTCTCTGACCCA	0%
WBC	N/A	N/A	N/A	N/A		N/A	N/A	0.10%
WPT	N/A	N/A	N/A	N/A		N/A	N/A	0%

UNITED STATES PATENT AND TRADEMARK OFFICE
DOCUMENT CLASSIFICATION BARCODE SHEET

New International
Application

Claim(s)

7

Index 1.1.5.2
Version 1.0
Rev 12/06/01

Section

We claim:

1.   A method of assessing the immune status of an individual comprising detecting the expression
      level of one or more genes expressed at different levels depending upon the rate of
      hematopoiesis or the distribution of hematopoietic cells along their maturation pathway in said
      individual.

2.   The method of claim 1, wherein said one or more genes comprise a nucleotide selected from a
      nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ
      ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ
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3.   The method of claim 2, wherein said expression level is detected by measuring the RNA level
        expressed by said one or more genes.

4.   The method of claim 3, wherein said RNA level is detected by PCR.

5.   The method of claim 3, wherein said RNA level is detected by hybridization.

6.   The method of claim 1, wherein said expression level is detected by measuring one or more
        proteins expressed by said one or more genes.

7.   A method of diagnosing or monitoring transplant rejection in an individual comprising
        detecting a rate of hematopoiesis.

8.   The method of claim 7, wherein said detecting is applied directly to the individual.

9.   The method of claim 7, wherein said detecting is applied to a sample isolated from the
        individual.

10.   The method of claim 7, wherein said detecting is selected from the group consisting of: RNA
        profiling assay, immunoassay, fluorescent activated cell sorting, protein assay, MRI imaging,
        bone marrow aspiration, and nuclear imaging.

11.   The method of claim 10, wherein said RNA profile assay is a PCR based assay.

12.   The method of claim 10, wherein said RNA profile assay is a hybridization based assay.

13.   The method of claim 10, wherein said RNA profile assay further comprises detecting the
        expression level of one or more genes in said individual where said one or more genes
        comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID
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14. The method of claim 7, wherein said transplant rejection is selected from the group consisting of: heart transplant rejection, kidney transplant rejection, liver transplant rejection, pancreas transplant rejection, pancreatic islet transplant rejection, lung transplant rejection, bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and mechanical organ replacement rejection.

15. The method of claim 7, wherein said transplant rejection is heart transplant.

16. The method of claim 7, wherein said transplant rejection is liver transplant.

17. The method of claim 7, wherein said transplant rejection is kidney transplant.

18. The method of claim 7, wherein said transplant rejection is bone marrow transplant.

19. The method of claim 7, wherein said transplant rejection is pancreatic islet transplant.

20. The method of claim 7, wherein said transplant rejection is stem cell transplant.

21. A method of diagnosing or monitoring transplant rejection in an individual comprising detecting a rate of hematopoiesis or the distribution of hematopoietic cells along their maturation pathway, wherein said detecting is selected from the group consisting of: RNA profiling assay, immunoassay, fluorescent activated cell sorting, protein assay, MRI imaging, bone marrow aspiration, and nuclear imaging.

22. The method of claim 21, wherein said RNA profile assay is a PCR based assay.

23. The method of claim 21, wherein said RNA profile assay is a hybridization based assay.

24. The method of claim 21, wherein said RNA profile assay further comprises detecting the expression level of one or more genes in said individual where said one or more genes comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53,

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NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, SEQ ID NO:319, SEQ ID NO:320, SEQ ID NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:2697, SEQ ID NO:2645, SEQ ID NO:2707, SEQ ID NO:2679, SEQ ID NO:2717, SEQ ID NO:2646, SEQ ID NO:2667, SEQ ID NO:2706, SEQ ID NO:2740, SEQ ID NO:2669, SEQ ID NO:2674, SEQ ID NO:2743, SEQ ID NO:2716, SEQ ID NO:2727, SEQ ID NO:2721, SEQ ID NO:2641, SEQ ID NO:2671, SEQ ID NO:2752, SEQ ID NO:2737, SEQ ID NO:2719, SEQ ID NO:2684, SEQ ID NO:2677, SEQ ID NO:2748, SEQ ID NO:2703, SEQ ID NO:2711, SEQ ID NO:2663, SEQ ID NO:2657, SEQ ID NO:2683, SEQ ID NO:2686, SEQ ID NO:2687, SEQ ID NO:2644, SEQ ID NO:2664, SEQ ID NO:2747, SEQ ID NO:2744, SEQ ID NO:2678, SEQ ID NO:2731, SEQ ID NO:2713, SEQ ID NO:2736, SEQ ID NO:2708, SEQ ID NO:2670, SEQ ID NO:2661, SEQ ID NO:2680, SEQ ID NO:2754, SEQ ID NO:2728, SEQ ID NO:2742, SEQ ID NO:2668, SEQ ID NO:2750, SEQ ID NO:2746, SEQ ID NO:2738, SEQ ID NO:2627, SEQ ID NO:2739, SEQ ID NO:2647, SEQ ID NO:2628, SEQ ID NO:2638, SEQ ID NO:2725, SEQ ID NO:2714, SEQ ID NO:2635, SEQ ID NO:2751, SEQ ID NO:2629, SEQ ID NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696, SEQ ID NO:2676, SEQ ID NO:2701, SEQ ID NO:2730, SEQ ID NO:2710, SEQ ID NO:2632, SEQ ID NO:2724, SEQ ID NO:2698, SEQ ID NO:2662, SEQ ID NO:2753, SEQ ID NO:2704, SEQ ID NO:2675, SEQ ID NO:2700, SEQ ID NO:2640, SEQ ID NO:2723, SEQ ID NO:2658, SEQ ID NO:2688, SEQ ID NO:2735, SEQ ID NO:2702, SEQ ID NO:2681, SEQ ID NO:2755, SEQ ID NO:2715, SEQ ID NO:2732, SEQ ID NO:2652, SEQ ID NO:2651, SEQ ID NO:2718, SEQ ID NO:2673, SEQ ID NO:2733, SEQ ID NO:2712, SEQ ID NO:2659, SEQ ID NO:2654, SEQ ID NO:2636, SEQ ID NO:2639, SEQ ID NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666, SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ

ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749,
SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID
NO:2709, SEQ ID NO:2653, SEQ ID NO:2729.

25.   The method of claim 21, wherein said transplant rejection is selected from the group
consisting of: heart transplant rejection, kidney transplant rejection, liver transplant rejection,
pancreas transplant rejection, pancreatic islet transplant rejection, lung transplant rejection,
bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and
mechanical organ replacement rejection.

26.   The method of claim 21, wherein said transplant rejection is heart transplant.

27.   The method of claim 21, wherein said transplant rejection is liver transplant.

28.   The method of claim 21, wherein said transplant rejection is kidney transplant.

29.   The method of claim 21, wherein said transplant rejection is bone marrow transplant.

30.   The method of claim 21, wherein said transplant rejection is pancreatic islet transplant.

31.   The method of claim 21, wherein said transplant rejection is stem cell transplant.

32.   A method of diagnosing or monitoring transplant rejection in a patient, comprising detecting
the expression level of one or more genes in said patient to diagnose or monitor transplant
rejection in said patient wherein said one or more genes comprise a nucleotide sequence
selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID
NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID.NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID
NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17,
SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID
NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28,
SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID
NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID
NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50,
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NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61,
SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID
NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72,
SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID
NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91,
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NO:2695, SEQ ID NO:2741, SEQ ID NO:2691, SEQ ID NO:2726, SEQ ID NO:2722, SEQ
ID NO:2689, SEQ ID NO:2734, SEQ ID NO:2631, SEQ ID NO:2656, SEQ ID NO:2696,
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NO:2690, SEQ ID NO:2705, SEQ ID NO:2685, SEQ ID NO:2692, SEQ ID NO:2693, SEQ
ID NO:2648, SEQ ID NO:2650, SEQ ID NO:2720, SEQ ID NO:2660, SEQ ID NO:2666,
SEQ ID NO:2699, SEQ ID NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID
NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ ID NO:2745, SEQ ID NO:2643, SEQ
ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637,
SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729.

33.   The method of claim 32, further comprising detecting the expression level of one or more
        additional genes in said patient to diagnose or monitor transplant rejection in a patient,
        wherein said one or more additional genes comprise a nucleotide sequence selected from the
        group consisting of: SEQ ID NO:8, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID
        NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:97,
        SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ
        ID NO:113, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID
        NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID
        NO:149, SEQ ID NO:150, SEQ ID NO:151.

34.   A method of diagnosing or monitoring transplant rejection in a patient, comprising detecting
        the expression level of one or more genes in said patient to diagnose or monitor transplant
        rejection in said patient wherein said one or more genes comprise a nucleotide sequence
        selected from the group consisting of SEQ ID NO: 36, 87, 94, 107, and 91.

35.   The method of claim 34 wherein said nucleotide sequence is SEQ ID NO: 36.

36.   The method of claim 34 wherein said nucleotide sequence is SEQ ID NO: 87.

37.   The method of claim 34 wherein said nucleotide sequence is SEQ ID NO: 94.

38.   The method of claim 34 wherein said nucleotide sequence is SEQ ID NO: 107.

39.   The method of claim 34 wherein said nucleotide sequence is SEQ ID NO: 91.

40.   A method of diagnosing or monitoring cardiac transplant rejection in a patient, comprising detecting the expression level of one or more genes in said patient to diagnose or monitor cardiac transplant rejection in said patient wherein said one or more genes comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID

NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID

NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID

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NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID

NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID

NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID

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NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID

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NO:321, SEQ ID NO:322, SEQ ID NO:323, SEQ ID NO:324, SEQ ID NO:325, SEQ ID

NO:326, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID

NO:331, SEQ ID NO:332.

41.   The method of claim 40, further comprising detecting the expression level of one or more
        additional genes in said patient to diagnose or monitor cardiac transplant rejection in a patient,
        wherein said one or more additional genes comprise a nucleotide sequence selected from the
        group consisting of: SEQ ID NO:8, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID
        NO:79, SEQ ID NO:97, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID
        NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID
        NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151.

42.   A method of diagnosing or monitoring kidney transplant rejection in a patient, comprising
        detecting the expression level of one or more genes in said patient to diagnose or monitor
        kidney transplant rejection in said patient wherein said one or more genes comprise a
        nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ
        ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ
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NO:2633, SEQ ID NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ
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SEQ ID NO:2665, SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID
NO:2709, SEQ ID NO:2653, SEQ ID NO:2729.

43.   The method of claim 42, further comprising detecting the expression level of one or more
        additional genes in said patient to diagnose or monitor kidney transplant rejection in a patient,
        wherein said one or more additional genes comprise a nucleotide sequence selected from the
        group consisting of: SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ
        ID NO:80, SEQ ID NO:81, SEQ ID NO:89, SEQ ID NO:99, SEQ ID NO:100, SEQ ID
        NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:140, SEQ ID
        NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID
        NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID
        NO:151.

44.   The method of claim 32 comprising detecting the expression level of at least two of said
        genes.

45.   The method of claim 32 comprising detecting the expression level of at least ten of said genes.

46.   The method of claim 32 comprising detecting the expression level of at least one hundred of
        said genes.

47.   The method of claim 32 comprising detecting the expression level of all said genes.

48.   The method of claim 32, wherein said transplant rejection is selected from the group
        consisting of: heart transplant rejection, kidney transplant rejection, liver transplant rejection,
        pancreas transplant rejection, pancreatic islet transplant rejection, lung transplant rejection,
        bone marrow transplant rejection, stem cell transplant rejection, xenotransplant rejection, and
        mechanical organ replacement rejection.

49.   The method of claim 32 wherein said transplant rejection is cardiac transplant rejection.

50.   The method of claim 32 wherein said transplant rejection is liver transplant rejection.

51.   The method of claim 32 wherein said transplant rejection is kidney transplant rejection.

52.   The method of claim 32 wherein said transplant rejection is bone marrow transplant rejection.

53.   The method of claim 32 wherein said transplant rejection is pancreatic islet transplant
        rejection.

54.   The method of claim 32 wherein said transplant rejection is stem cell transplant rejection.

55.   The method of claim 32 wherein said expression level is detected by measuring the RNA level
        expressed by said one or more genes.

56.   The method of claim 55, further including isolating RNA from said patient prior to detecting
        said RNA level expressed by said one or more genes.

57.   The method of claim 55 wherein said RNA level is detected by PCR.

58.   The method of claim 57 wherein said PCR uses primers consisting of nucleotide sequences
        selected from the group consisting of SEQ ID NO:665, SEQ ID NO:666, SEQ ID NO:667,
        SEQ ID NO:668, SEQ ID NO:669, SEQ ID NO:670, SEQ ID NO:671, SEQ ID NO:672, SEQ

ID NO:673, SEQ ID NO:674, SEQ ID NO:675, SEQ ID NO:676, SEQ ID NO:677, SEQ ID

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59.   The method of claim 58 wherein said PCR uses corresponding probes consisting of nucleotide sequences selected from the group consisting of SEQ ID NO:1327, SEQ ID NO:1328, SEQ ID NO:1329, SEQ ID NO:1330, SEQ ID NO:1331, SEQ ID NO:1332, SEQ ID NO:1333, SEQ ID NO:1334, SEQ ID NO:1335, SEQ ID NO:1336, SEQ ID NO:1337, SEQ ID NO:1338, SEQ ID NO:1339, SEQ ID NO:1340, SEQ ID NO:1341, SEQ ID NO:1342, SEQ ID NO:1343, SEQ ID NO:1344, SEQ ID NO:1345, SEQ ID NO:1346, SEQ ID NO:1347, SEQ ID NO:1348, SEQ ID NO:1349, SEQ ID NO:1350, SEQ ID NO:1351, SEQ ID NO:1352, SEQ ID NO:1353, SEQ ID NO:1354, SEQ ID NO:1355, SEQ ID NO:1356, SEQ ID NO:1357, SEQ ID NO:1358, SEQ ID NO:1359, SEQ ID NO:1360, SEQ ID NO:1361, SEQ ID NO:1362, SEQ ID NO:1363, SEQ ID NO:1364, SEQ ID NO:1365, SEQ ID NO:1366, SEQ ID NO:1367, SEQ ID NO:1368, SEQ ID NO:1369, SEQ ID NO:1370, SEQ ID NO:1371, SEQ ID NO:1372, SEQ ID NO:1373, SEQ ID NO:1374, SEQ ID NO:1375, SEQ ID NO:1376, SEQ ID NO:1377, SEQ ID NO:1378, SEQ ID NO:1379, SEQ ID NO:1380, SEQ ID NO:1381, SEQ ID NO:1382, SEQ ID NO:1383, SEQ ID NO:1384, SEQ ID NO:1385, SEQ ID NO:1386, SEQ ID NO:1387, SEQ ID NO:1388, SEQ ID NO:1389, SEQ ID NO:1390, SEQ ID NO:1391, SEQ ID NO:1392, SEQ ID NO:1393, SEQ ID NO:1394, SEQ ID NO:1395, SEQ ID NO:1396, SEQ ID NO:1397, SEQ ID NO:1398, SEQ ID NO:1399, SEQ ID NO:1400, SEQ ID NO:1401, SEQ ID NO:1402, SEQ ID NO:1403, SEQ ID NO:1404, SEQ ID NO:1405, SEQ ID NO:1406, SEQ ID NO:1407, SEQ ID NO:1408, SEQ ID NO:1409, SEQ ID NO:1410, SEQ ID NO:1411, SEQ ID NO:1412, SEQ ID NO:1413, SEQ ID NO:1414, SEQ ID NO:1415, SEQ ID NO:1416, SEQ ID NO:1417, SEQ ID NO:1418, SEQ ID NO:1419, SEQ ID NO:1420, SEQ ID NO:1421, SEQ ID NO:1422, SEQ ID NO:1423, SEQ ID NO:1424, SEQ ID NO:1425, SEQ ID NO:1426, SEQ ID NO:1427, SEQ ID NO:1428, SEQ ID NO:1429, SEQ ID NO:1430, SEQ ID NO:1431, SEQ ID NO:1432, SEQ ID NO:1433, SEQ ID NO:1434, SEQ ID NO:1435, SEQ ID NO:1436, SEQ ID NO:1437, SEQ ID NO:1438, SEQ ID NO:1439, SEQ ID NO:1440, SEQ ID NO:1441, SEQ ID NO:1442, SEQ ID NO:1443, SEQ ID NO:1444, SEQ ID NO:1445, SEQ ID NO:1446, SEQ ID NO:1447, SEQ ID NO:1448, SEQ ID NO:1449, SEQ ID NO:1450, SEQ ID NO:1451, SEQ ID NO:1452, SEQ ID NO:1454, SEQ ID NO:1455, SEQ ID NO:1456, SEQ ID NO:1457, SEQ ID NO:1458, SEQ ID NO:1459, SEQ ID NO:1460, SEQ ID NO:1461, SEQ ID NO:1462, SEQ ID NO:1463, SEQ ID NO:1464, SEQ ID NO:1465, SEQ ID NO:1466, SEQ ID NO:1467, SEQ ID NO:1468, SEQ ID NO:1469, SEQ ID NO:1470, SEQ ID NO:1471, SEQ ID NO:1472, SEQ ID NO:1473, SEQ ID NO:1474, SEQ ID NO:1475, SEQ ID NO:1476, SEQ ID NO:1477, SEQ ID NO:1478, SEQ ID NO:1479, SEQ ID NO:1480, SEQ ID NO:1481, SEQ ID NO:1482, SEQ ID NO:1483, SEQ ID NO:1484, SEQ ID NO:1485, SEQ ID NO:1486, SEQ ID NO:1487, SEQ ID NO:1488, SEQ ID NO:1489, SEQ ID NO:1490, SEQ ID NO:1491, SEQ ID NO:1492, SEQ ID NO:1493, SEQ ID NO:1494, SEQ ID NO:1495, SEQ ID NO:1496, SEQ ID NO:1497, SEQ ID

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ID NO:2396, SEQ ID NO:2397, SEQ ID NO:2398, SEQ ID NO:2399.

60.   The method of claim 55 wherein said RNA level is detected by hybridization.

61.   The method of claim 55 wherein said RNA level is detected by hybridization to an
        oligonucleotide.

62.   The method of claim 61 wherein said oligonucleotide consists of a nucleotide sequence
        selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID
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63.   The method of claim 61 wherein said oligonucleotide comprises DNA, RNA, cDNA, PNA,
       genomic DNA, or synthetic oligonucleotides.

64.   The method of claim 32 wherein said expression level is detected by measuring one or more
       proteins expressed by said one or more genes.

65.   The method of claim 64 wherein said one or more proteins comprise an amino acid sequence
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66. The method of claim 33 wherein said expression level of said one or more genes is detected by measuring one or more proteins expressed by said one or more genes, and said expression level of said one or more additional genes is detected by measuring one or more proteins expressed by said one or more additional genes.

67. The method of claim 66, wherein said one or more proteins expressed by said one or more genes comprise an amino acid sequence selected from the group consisting of SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510,

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NO:3006, SEQ ID NO:3007, SEQ ID NO:3008, SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID NO:3013, SEQ ID NO:3014, SEQ ID NO:3015, and said one or more proteins expressed by said one or more additional genes comprise an amino acid sequence selected from the group consisting of SEQ ID NO:2406, SEQ ID NO:2431, SEQ ID NO:2471, SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID NO:2474, SEQ ID NO:2475, SEQ ID NO:2476, SEQ ID NO:2477, SEQ ID NO:2484, SEQ ID NO:2487, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500, SEQ ID NO:2501, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ ID NO:2526, SEQ ID NO:2527.

68.   The method of claim 40 wherein said expression level is detected by measuring one or more proteins expressed by said one or more genes.

69.   The method of claim 68 wherein said one or more proteins comprise an amino acid sequence selected from the group consisting of SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ ID NO:2449, SEQ ID NO:2450, SEQ ID NO:2451, SEQ ID NO:2452, SEQ ID NO:2453, SEQ ID NO:2454, SEQ ID NO:2455, SEQ ID NO:2456, SEQ ID NO:2457, SEQ ID NO:2458, SEQ ID NO:2459, SEQ ID NO:2460, SEQ ID NO:2461, SEQ ID NO:2462, SEQ ID NO:2463, SEQ ID NO:2464, SEQ ID NO:2465, SEQ ID NO:2466, SEQ ID NO:2467, SEQ ID NO:2468, SEQ ID NO:2469, SEQ ID NO:2470, SEQ ID NO:2478, SEQ ID NO:2479, SEQ ID NO:2480, SEQ ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2485, SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521, SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID NO:2532, SEQ ID NO:2533, SEQ ID NO:2534, SEQ ID NO:2535, SEQ ID NO:2536, SEQ ID NO:2537, SEQ ID NO:2538, SEQ ID NO:2539, SEQ ID NO:2540, SEQ ID NO:2541, SEQ ID NO:2542, SEQ ID NO:2543, SEQ ID NO:2544, SEQ ID NO:2545, SEQ ID NO:2546, SEQ ID NO:2547, SEQ ID NO:2548, SEQ ID NO:2549, SEQ ID NO:2550, SEQ ID NO:2551,

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ID NO:2962, SEQ ID NO:2963, SEQ ID NO:2964, SEQ ID NO:2965, SEQ ID NO:2966,
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ID NO:2976, SEQ ID NO:2977, SEQ ID NO:2978, SEQ ID NO:2979, SEQ ID NO:2980,
SEQ ID NO:2981, SEQ ID NO:2982, SEQ ID NO:2983, SEQ ID NO:2984, SEQ ID
NO:2985, SEQ ID NO:2986, SEQ ID NO:2987, SEQ ID NO:2988, SEQ ID NO:2989, SEQ
ID NO:2990, SEQ ID NO:2991, SEQ ID NO:2992, SEQ ID NO:2993, SEQ ID NO:2994,
SEQ ID NO:2995, SEQ ID NO:2996, SEQ ID NO:2997, SEQ ID NO:2998, SEQ ID
NO:2999, SEQ ID NO:3000, SEQ ID NO:3001, SEQ ID NO:3002, SEQ ID NO:3003, SEQ
ID NO:3004, SEQ ID NO:3005, SEQ ID NO:3006, SEQ ID NO:3007, SEQ ID NO:3008,
SEQ ID NO:3009, SEQ ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID
NO:3013, SEQ ID NO:3014, SEQ ID NO:3015.

70.   The method of claim 41 wherein said expression level of said one or more genes is detected
        by measuring one or more proteins expressed by said one or more genes, and said expression
        level of said one or more additional genes is detected by measuring one or more proteins
        expressed by said one or more additional genes.

71.   The method of claim 70, wherein said one or more proteins expressed by said one or more
        genes comprise an amino acid sequence selected from the group consisting of SEQ ID
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        ID NO:2405, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409, SEQ ID NO:2410,
        SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID
        NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ
        ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424,
        SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID NO:2428, SEQ ID
        NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ ID NO:2434, SEQ
        ID NO:2435, SEQ ID NO:2436, SEQ ID NO:2437, SEQ ID NO:2438, SEQ ID NO:2439,
        SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID NO:2443, SEQ ID
        NO:2444, SEQ ID NO:2445, SEQ ID NO:2446, SEQ ID NO:2447, SEQ ID NO:2448, SEQ
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        ID NO:2481, SEQ ID NO:2482, SEQ ID NO:2483, SEQ ID NO:2484, SEQ ID NO:2485,
        SEQ ID NO:2486, SEQ ID NO:2488, SEQ ID NO:2489, SEQ ID NO:2490, SEQ ID
        NO:2491, SEQ ID NO:2492, SEQ ID NO:2493, SEQ ID NO:2494, SEQ ID NO:2495, SEQ
        ID NO:2496, SEQ ID NO:2497, SEQ ID NO:2498, SEQ ID NO:2499, SEQ ID NO:2500,
        SEQ ID NO:2501, SEQ ID NO:2502, SEQ ID NO:2503, SEQ ID NO:2504, SEQ ID
        NO:2505, SEQ ID NO:2506, SEQ ID NO:2507, SEQ ID NO:2508, SEQ ID NO:2509, SEQ
        ID NO:2510, SEQ ID NO:2511, SEQ ID NO:2512, SEQ ID NO:2513, SEQ ID NO:2514,
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NO:2609, SEQ ID NO:2610, SEQ ID NO:2611, SEQ ID NO:2612, SEQ ID NO:2613, SEQ
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SEQ ID NO:2619, SEQ ID NO:2620, SEQ ID NO:2621, SEQ ID NO:2622, SEQ ID
NO:2623, SEQ ID NO:2624, SEQ ID NO:2625, SEQ ID NO:2626, and
said one or more protein expressed by said one or more additional genes comprise an amino
acid sequence selected from the group consisting of SEQ ID NO:2406, SEQ ID NO:2431,
SEQ ID NO:2472, SEQ ID NO:2473, SEQ ID NO:2474, SEQ ID NO:2475, SEQ ID
NO:2487, SEQ ID NO:2522, SEQ ID NO:2523, SEQ ID NO:2524, SEQ ID NO:2525, SEQ
ID NO:2526, SEQ ID NO:2527.

72.   The method of claim 42 wherein said expression level is detecting by measuring one or more
       proteins encoded by said one or more genes.

73.   The method of claim 72 wherein said one or more proteins comprise an amino acid sequence
       selected from the group consisting of [SEQ ID NO:2400, SEQ ID NO:2401, SEQ ID
       NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ ID NO:2405, SEQ ID NO:2406, SEQ
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       SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID NO:2414, SEQ ID NO:2415, SEQ ID
       NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ ID NO:2419, SEQ ID NO:2420, SEQ
       ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423, SEQ ID NO:2424, SEQ ID NO:2425,
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ID NO:2937, SEQ ID NO:2938, SEQ ID NO:2939, SEQ ID NO:2941, SEQ ID NO:2942,
SEQ ID NO:2943, SEQ ID NO:2945, SEQ ID NO:2946, SEQ ID NO:2947, SEQ ID
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ID NO:3010, SEQ ID NO:3011, SEQ ID NO:3012, SEQ ID NO:3013, SEQ ID NO:3014,
SEQ ID NO:3015.

74.   The method of claim 43 wherein said expression level of said one or more genes is detected
       by measuring one or more proteins expressed by said one or more genes, and said expression
       level of said one or more additional genes is detected by measuring one or more proteins
       expressed by said one or more additional genes.

75.   The method of claim 74, wherein said one or more proteins expressed by said one or more
       genes comprises an amino acid sequence selected from the group consisting of SEQ ID
       NO:2400, SEQ ID NO:2401, SEQ ID NO:2402, SEQ ID NO:2403, SEQ ID NO:2404, SEQ
       ID NO:2405, SEQ ID NO:2406, SEQ ID NO:2407, SEQ ID NO:2408, SEQ ID NO:2409,
       SEQ ID NO:2410, SEQ ID NO:2411, SEQ ID NO:2412, SEQ ID NO:2413, SEQ ID
       NO:2414, SEQ ID NO:2415, SEQ ID NO:2416, SEQ ID NO:2417, SEQ ID NO:2418, SEQ
       ID NO:2419, SEQ ID NO:2420, SEQ ID NO:2421, SEQ ID NO:2422, SEQ ID NO:2423,
       SEQ ID NO:2424, SEQ ID NO:2425, SEQ ID NO:2426, SEQ ID NO:2427, SEQ ID
       NO:2428, SEQ ID NO:2429, SEQ ID NO:2430, SEQ ID NO:2432, SEQ ID NO:2433, SEQ
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       SEQ ID NO:2439, SEQ ID NO:2440, SEQ ID NO:2441, SEQ ID NO:2442, SEQ ID
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       ID NO:2503, SEQ ID NO:2504, SEQ ID NO:2505, SEQ ID NO:2506, SEQ ID NO:2507,
       SEQ ID NO:2508, SEQ ID NO:2509, SEQ ID NO:2510, SEQ ID NO:2511, SEQ ID
       NO:2512, SEQ ID NO:2513, SEQ ID NO:2514, SEQ ID NO:2515, SEQ ID NO:2516, SEQ
       ID NO:2517, SEQ ID NO:2518, SEQ ID NO:2519, SEQ ID NO:2520, SEQ ID NO:2521,
       SEQ ID NO:2528, SEQ ID NO:2529, SEQ ID NO:2530, SEQ ID NO:2531, SEQ ID
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76. The method of claim 64, wherein said measuring comprises measuring serum.

77. The method of claim 64, wherein said protein is a cell surface protein.

78. The method of claim 64, wherein said measuring comprises using a fluorescent activated cell sorter

79.   A substantially purified oligonucleotide having the nucleotide sequence selected from the
        group consisting of [SEQ ID NO: X + Y – novel gene sequences + literature sequences].

80.   A substantially purified oligonucleotide having the nucleotide sequence selected from the
        group consisting of [CHECK TO BE SURE THESE ARE THE CORRECT
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NO:662, SEQ ID NO:663, SEQ ID NO:664.

81. An oligonucleotide comprising a nucleotide sequence having at least 90% sequence identity to
said oligonucleotide of claim 79.

82. An oligonucleotide comprising a nucleotide sequence having at least 90% sequence identity to
said oligonucleotide of claim 80.

83. An oligonucleotide comprising a nucleotide sequence that hybridizes at high stringency to said
oligonucleotide of claim 79.

84. An oligonucleotide comprising a nucleotide sequence that hybridizes at high stringency to said
oligonucleotide of claim 80.

85.   The diagnostic oligonucleotide of claim 79, wherein said nucleotide sequence comprises DNA, cDNA, PNA, genomic DNA, or synthetic oligonucleotides.

86.   The method of claim 32, wherein the expression level detected is expression level in the patient's bodily fluid.

87.   The method of claim 86, wherein said bodily fluid is peripheral blood.

88.   A method of diagnosing or monitoring transplant rejection in a patient, comprising detecting the expression level of four or more genes in said patient to diagnose or monitor transplant rejection in said patient wherein said four or more genes comprise a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID

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NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ

ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665,

SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID

NO:2653, SEQ ID NO:2729.

89.   A method of diagnosing or monitoring kidney transplant rejection in a patient, comprising

detecting one or more proteins in a bodily fluid of said patient to diagnose or monitor

transplant rejection in said patient wherein said one or more proteins comprise a protein

sequence selected from the group consisting of SEQ ID NO:76, SEQ ID NO:2663, SEQ ID

NO:98, SEQ ID NO:2696, SEQ ID NO:2736, SEQ ID NO:2751, SEQ ID NO:2631, SEQ ID

NO:2675, SEQ ID NO:2700, and SEQ ID NO:2693.

90.   A system for detecting gene expression in body fluid comprising at least two isolated

polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the

gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:2,

SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9,

SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID

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NO:2672, SEQ ID NO:2642, SEQ ID NO:2682, SEQ ID NO:2655, SEQ ID NO:2630, SEQ

ID NO:2745, SEQ ID NO:2643, SEQ ID NO:2694, SEQ ID NO:2749, SEQ ID NO:2665,

SEQ ID NO:2649, SEQ ID NO:2637, SEQ ID NO:2634, SEQ ID NO:2709, SEQ ID

NO:2653, SEQ ID NO:2729 and the gene is differentially expressed in body fluid in an

individual rejecting a transplanted organ compared to the expression of the gene in leukocytes

in an individual not rejecting a transplanted organ.

91. A system for detecting gene expression in body fluid comprising at least two isolated polynucleotides wherein the isolated polynucleotides detect expression of a gene wherein the gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID

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SEQ ID NO:2709, SEQ ID NO:2653, SEQ ID NO:2729 and the gene expression is related to
the rate of hematopoiesis or the distribution of hematopoeitic cells along their maturation
pathway.

Figure 1: Novel Gene Sequence Analysis
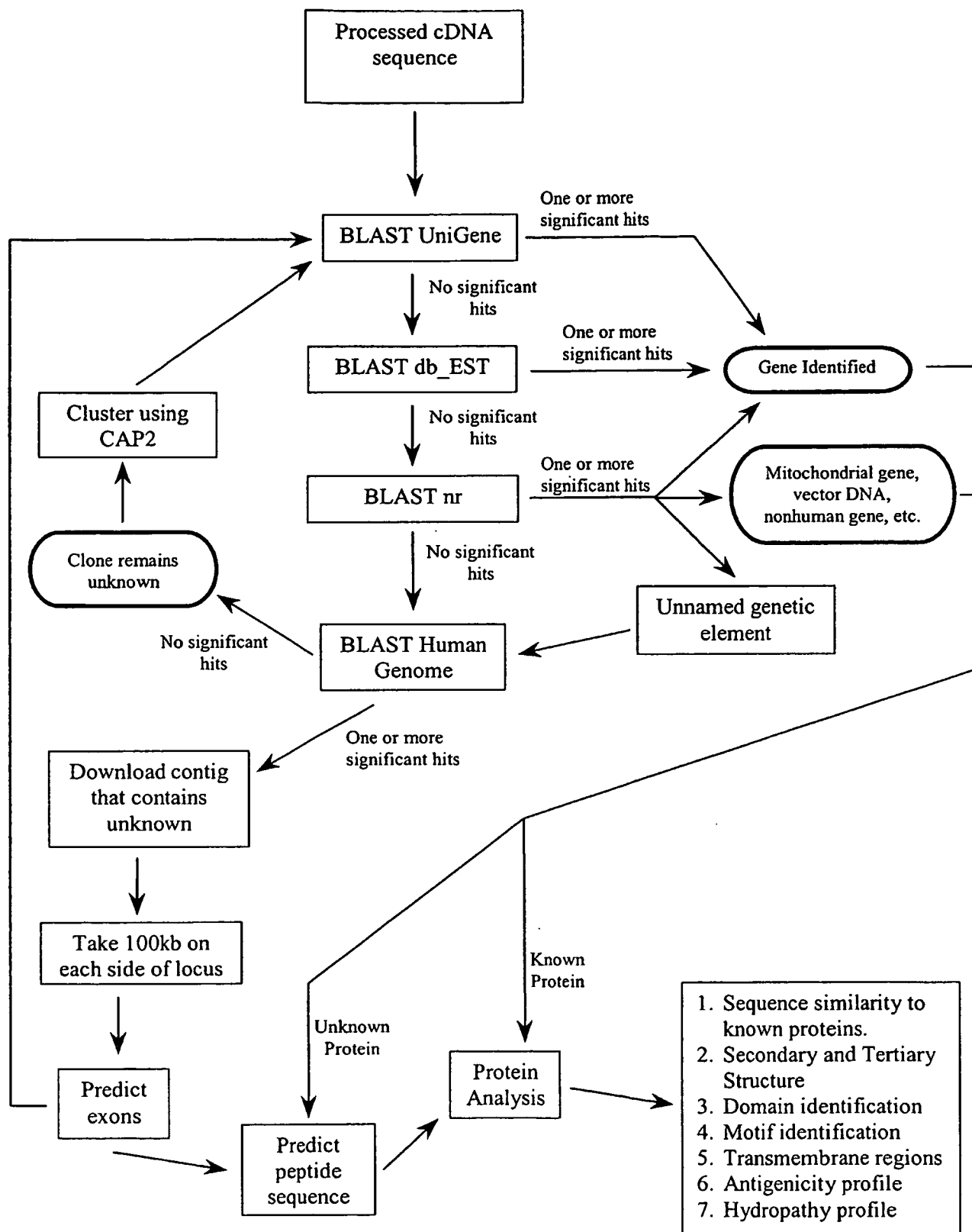
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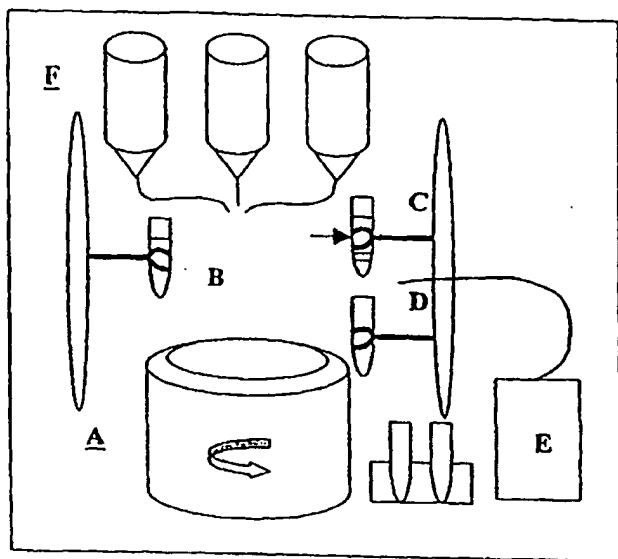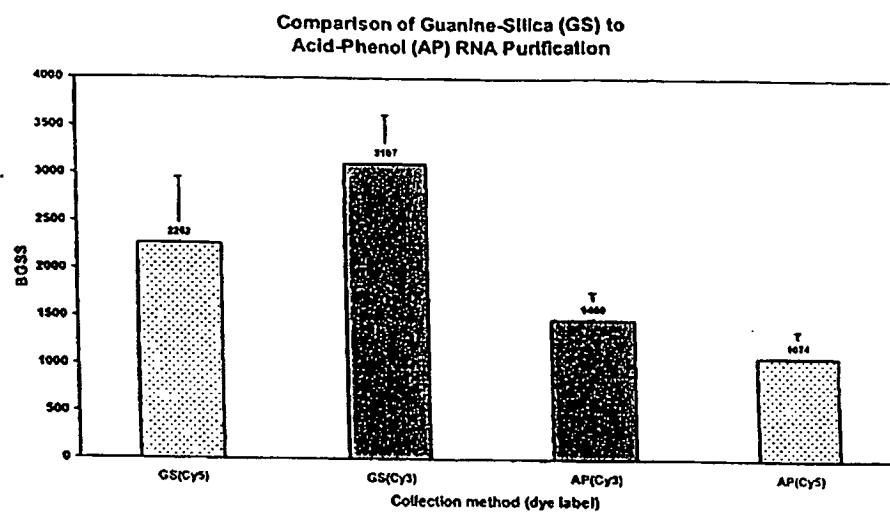
FIGURE 3

Comparison of Guanine-Silica (GS) to
Acid-Phenol (AP) RNA Purification

FIGURE 4

Expression of Leukocyte Specific Genes

FIGURE 5

Expression of Leukocyte-Specific Genes

FIGURE 6

Comparison of Control RNAs

All columns use the same scale.

——— Mononuclear cells, resting and stimulated

——— 10 Buffy Coats, resting

——— Mononuclear cells, resting

All markers are connected and ordered by Features.

10 µg of each control RNA was labeled.
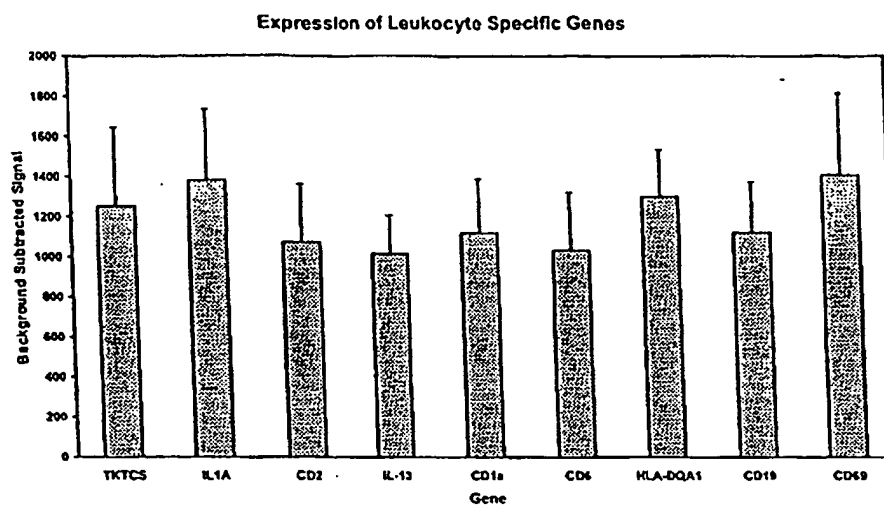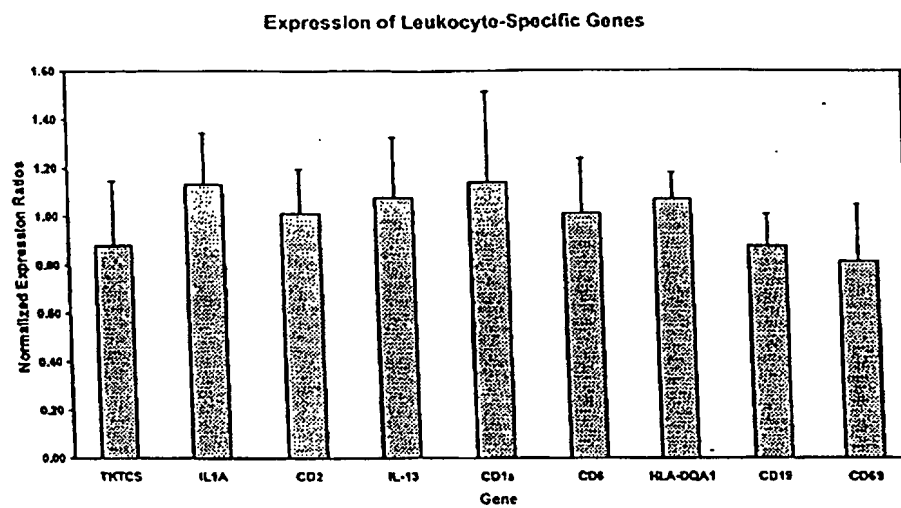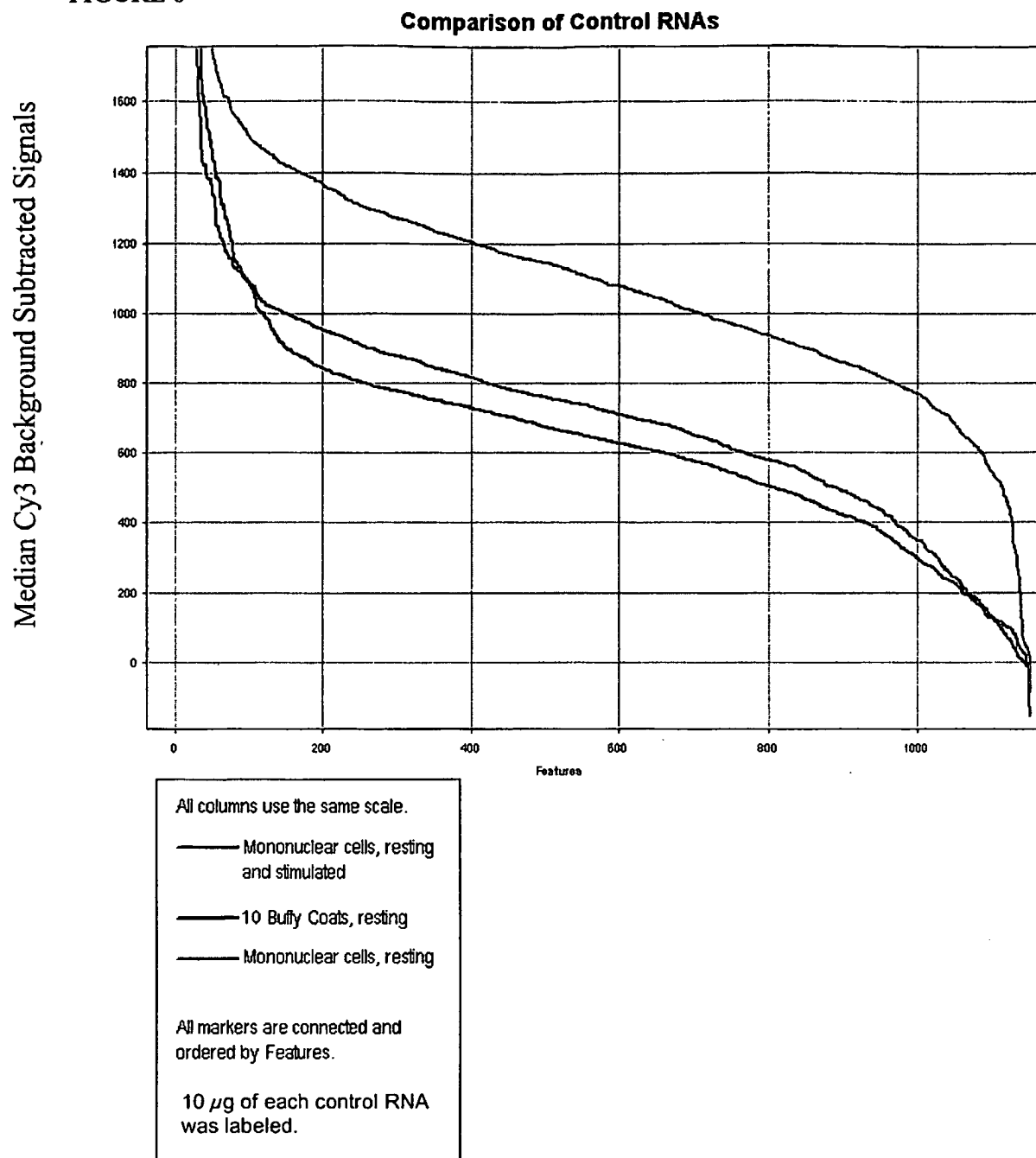
Figure 7: Cardiac Allograft rejection diagnostic genes.

A.

Sample	Grade	Marker Gene Expression Ratios				
		3020	3019	2760	3018	85
12-0025-02	0	3.90	3.69	5.49	3.24	3.34
12-0024-04	0	3.66	4.05	5.89	3.75	3.03
15-0024-01	0	3.55	4.01	5.61	2.90	3.23
12-0029-03	0	3.44	3.12	4.25	3.55	3.07
12-0024-03	0	2.88	2.54	2.56	2.20	2.38
14-0021-05	0	1.31	1.03	1.07	0.91	0.99
14-0005-06	3A	0.42	0.27	0.51	0.22	0.26
14-0012-07	3A	0.60	0.62	0.70	0.42	0.61
14-0001-06	3A	0.93	0.71	0.58	0.37	0.44
14-0009-01	3A	0.71	0.63	0.68	0.61	0.66
12-0012-02	3A	0.86	0.85	0.73	0.41	0.72
12-0001-01	3A	1.08	0.97	1.01	0.40	1.06
Average Grade 0:		3.13	3.07	4.14	2.76	2.67
Average Grade 3A:		0.77	0.68	0.70	0.40	0.62
Fold Difference:		4.08	4.55	5.91	6.82	4.28

B. **CART classification model.**

Is the static expression
of gene 223 (EST)
≤ 0.0883?

Y   N

Is the referenced
expression of gene
3017 (GABPB2) ≤ -0.0105?

Is the referenced
expression of gene
2756 (Granzyme B) ≤ -

Y   N   Y   N

Rejection
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15 Rejection

No Rejection
5 No Rejection
0 Rejection

Rejection
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1 Rejection

No Rejection
12 No Rejection
0 Rejection
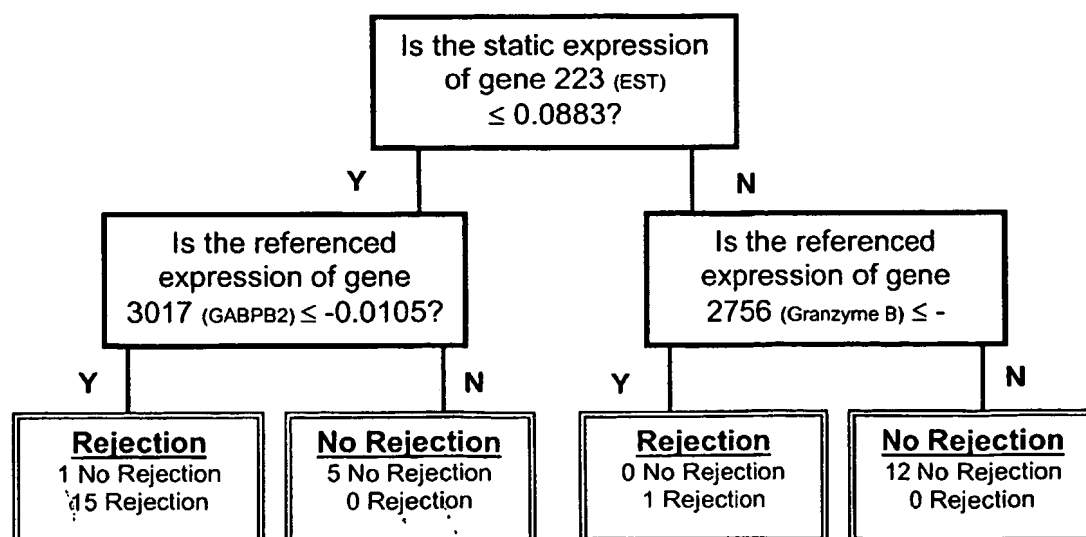
C. **Surrogates for the CART classification model.**

Primary Splitter	static 223	ref 3017	ref 4
Surrogate 1	ref 167	ref 102	ref 2761
Surrogate 2	ref 3016	static 36	ref 2762
Surrogate 3	ref 1760	ref 2764	ref 3016
Surrogate 4	ref 85	ref 2759	ref 2757
Surrogate 5	ref 2763	ref 2761	ref 2758

Figure 8A: Validation of differential expression of Granzyme B in CMV patients using Real-time PCR

Figure 8B.

QPCR of Granzyme B

Figure 9

A.

B.

C.

D.

Figure 10

Figure 11

Variation of Control Genes from PAX RNA
(2ug) and CPT RNA (0.5 ug)

Intensity of Control Genes from PAX RNA
(2ug) and CPT RNA (0.5 ug)
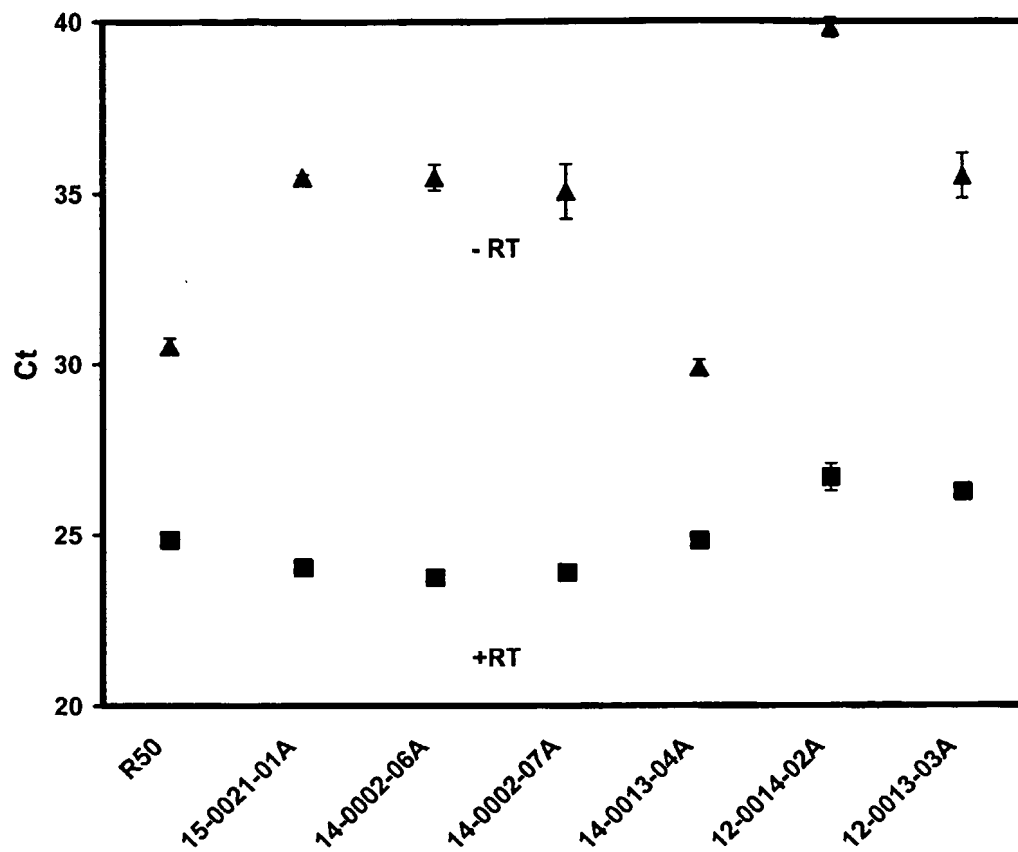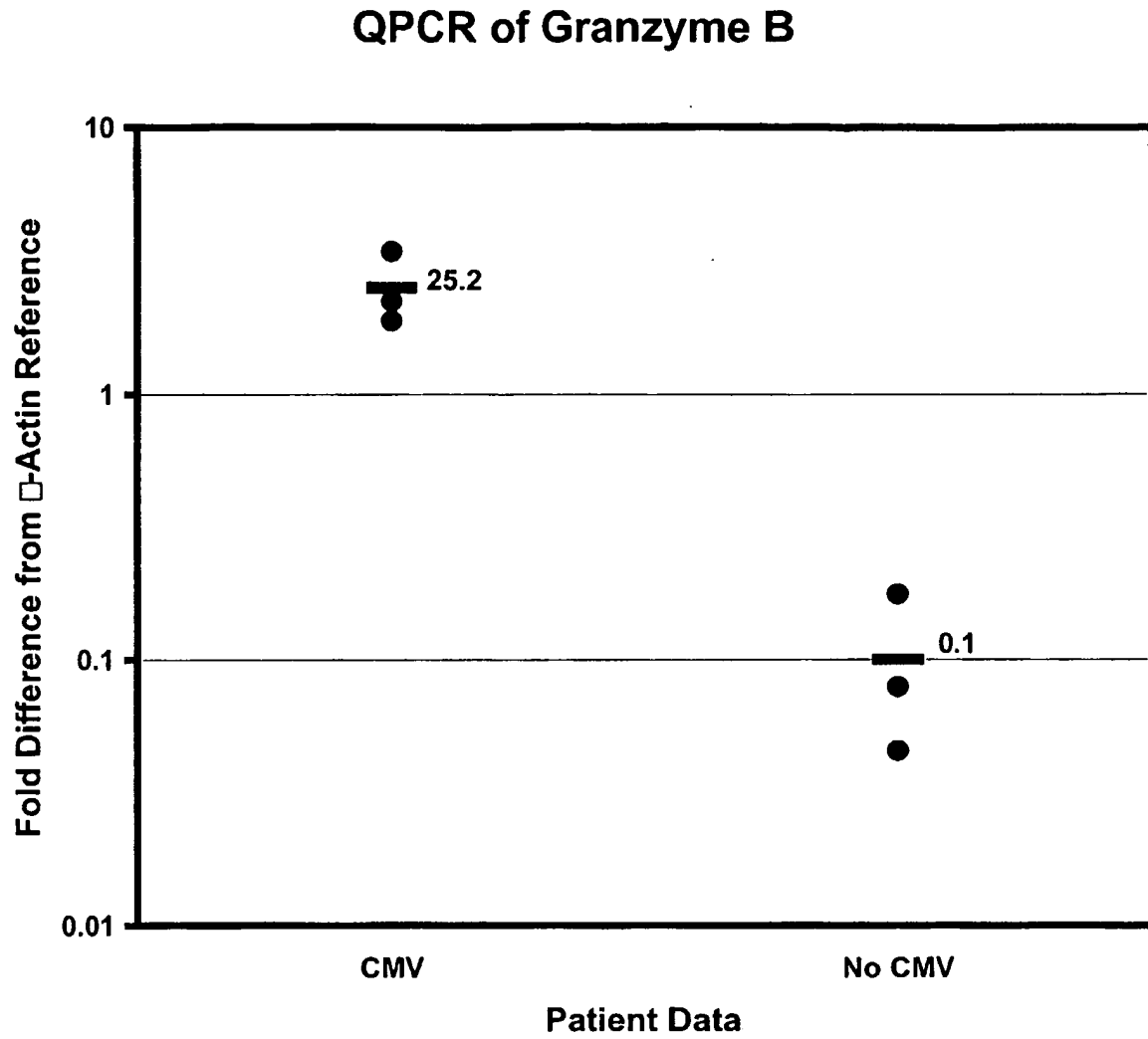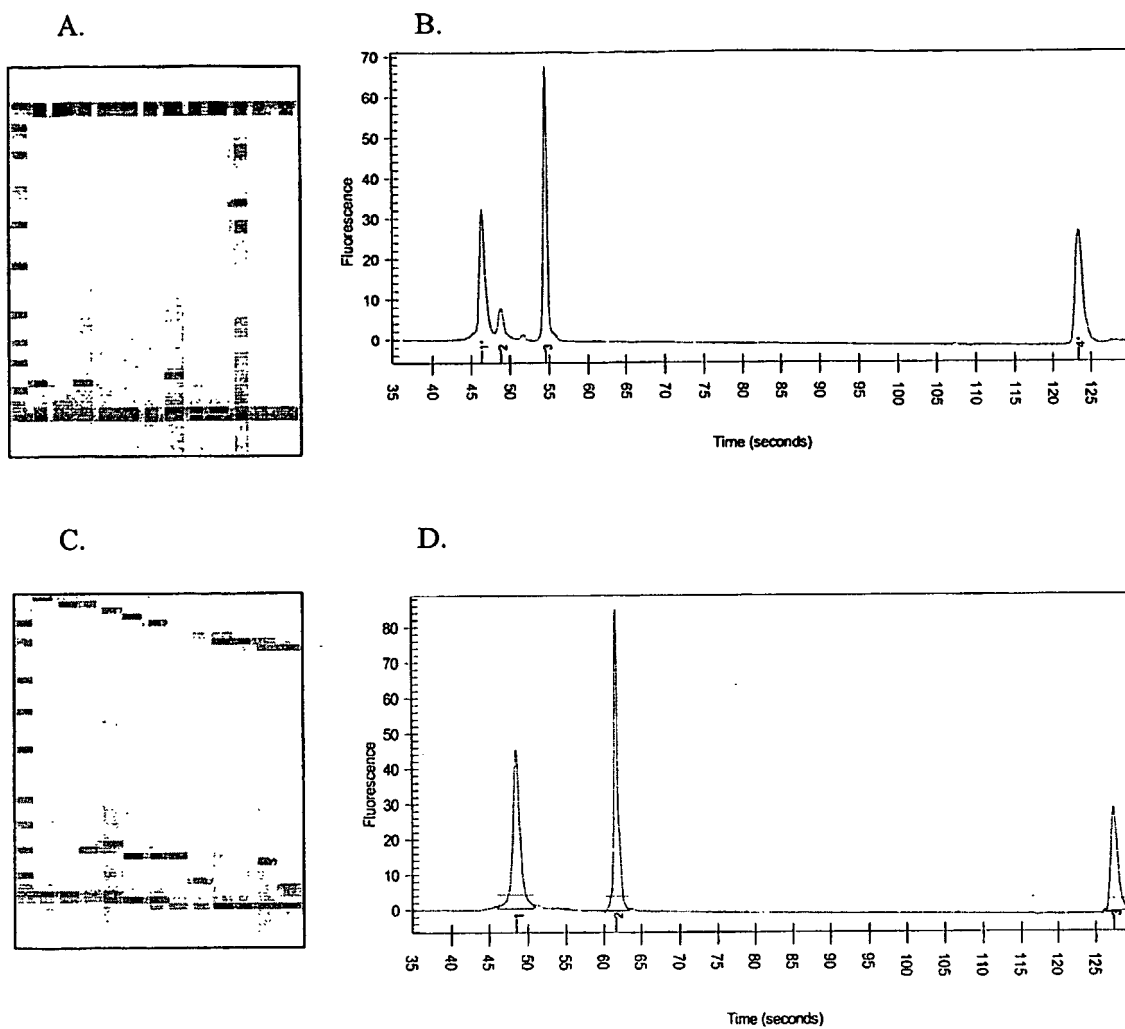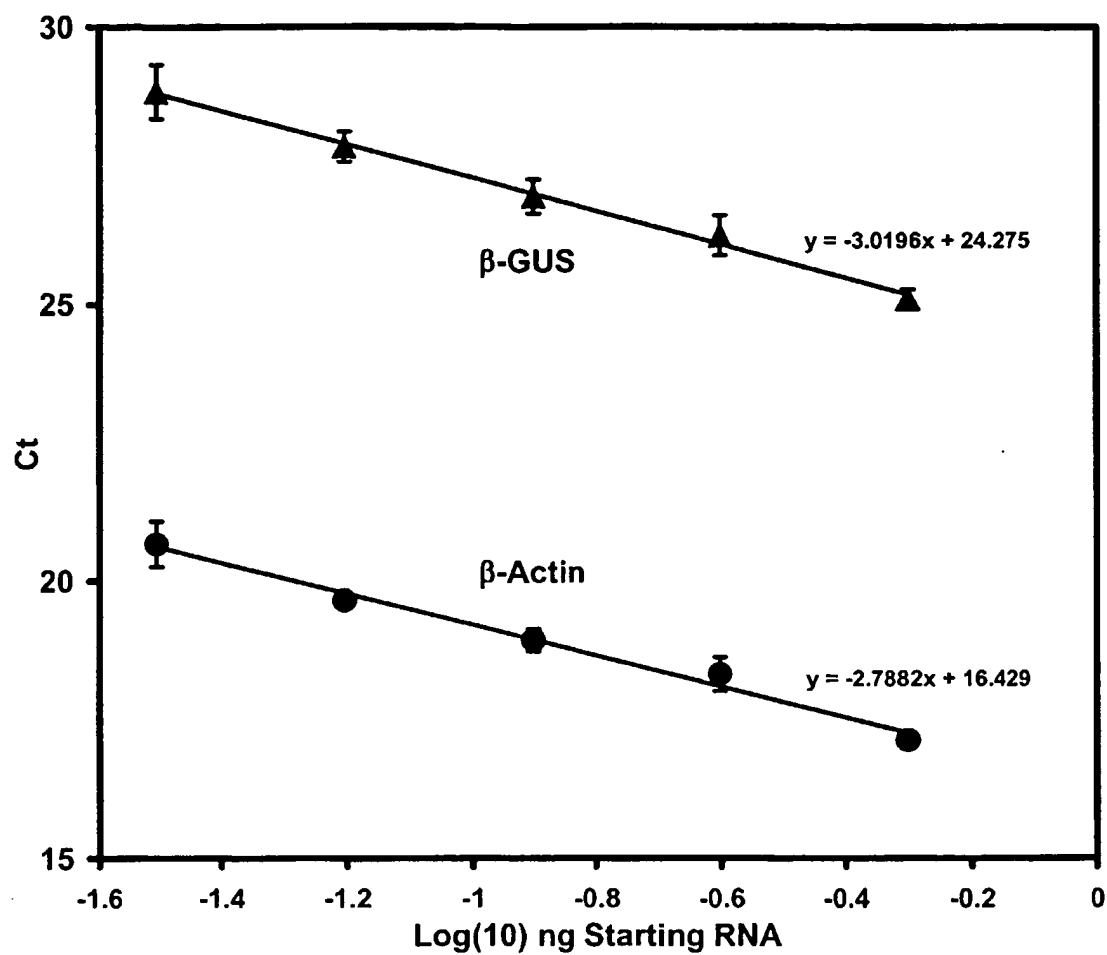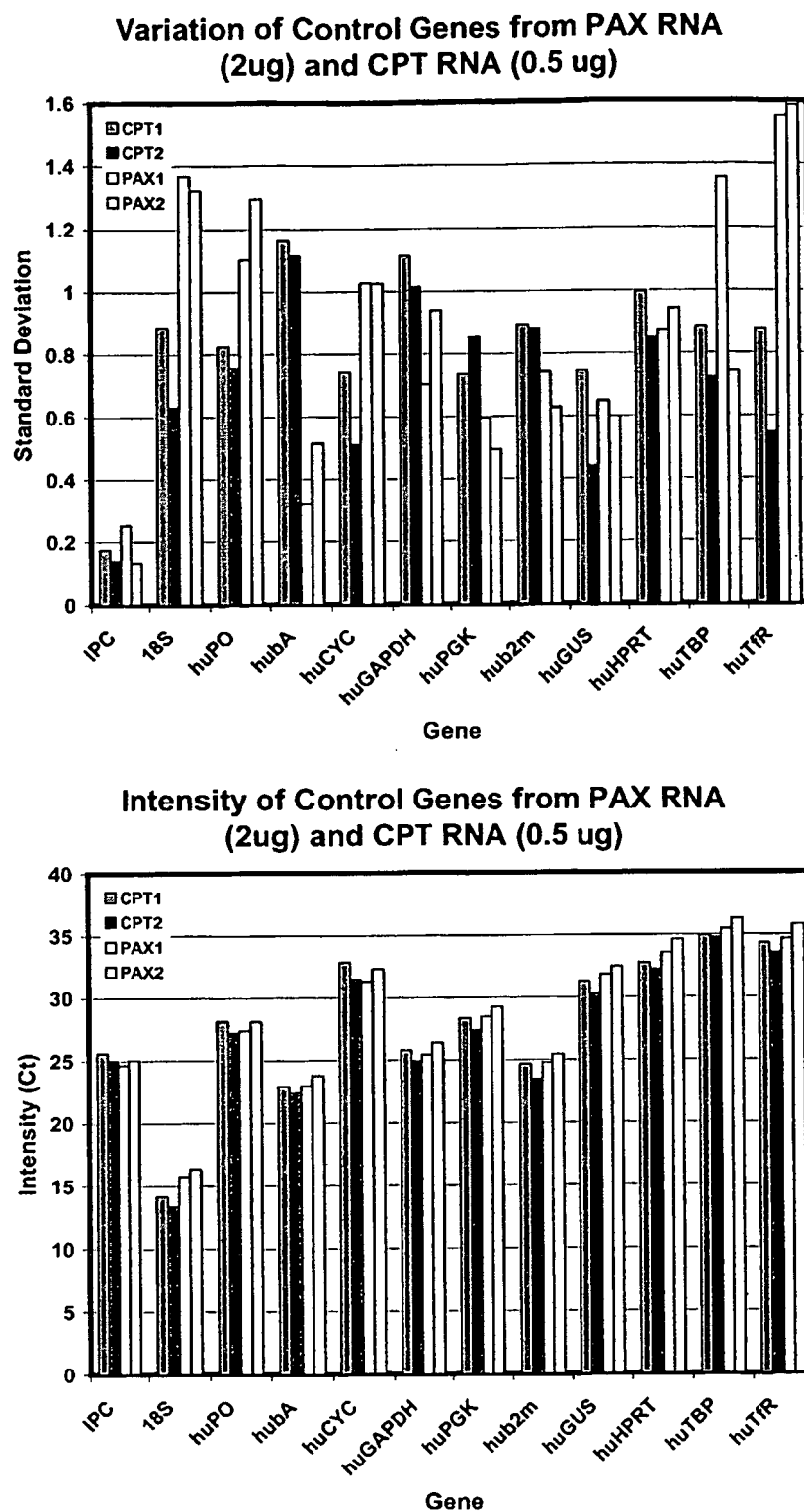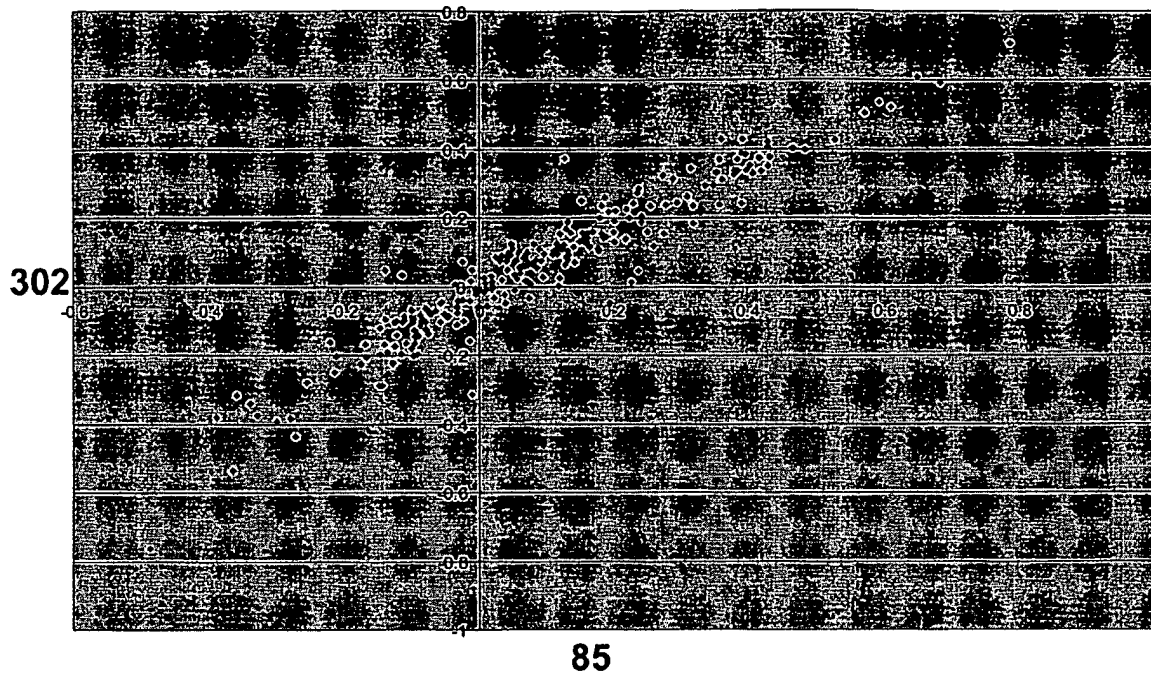
Figure 12

Figure 13
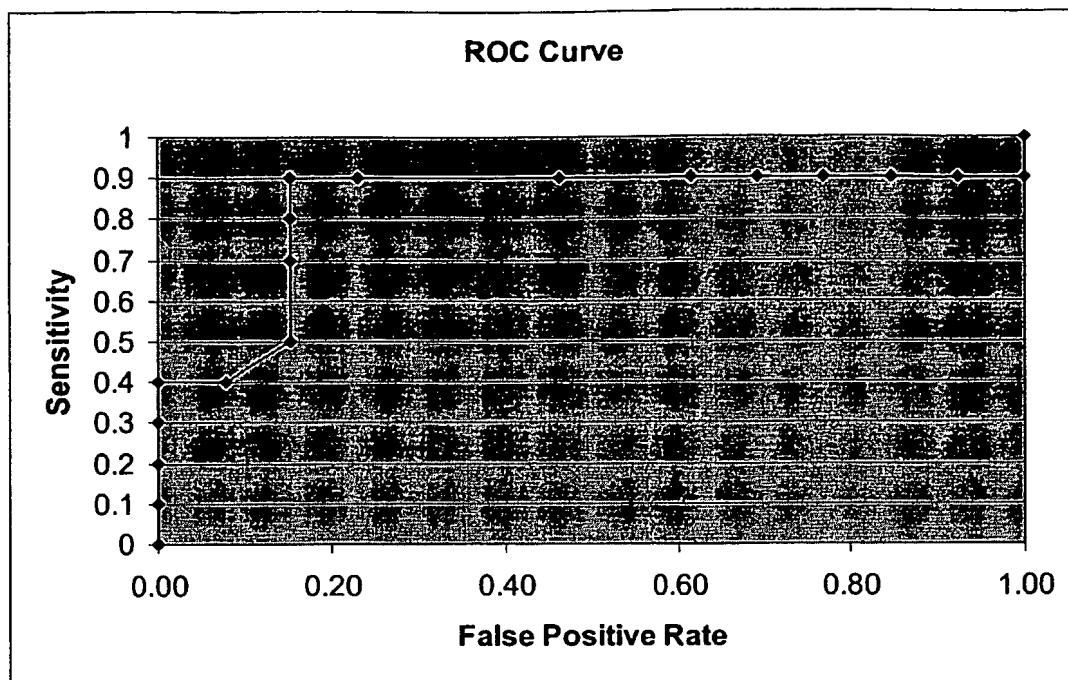
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<213>  Homo sapiens

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<212>  DNA
<213>  Homo sapiens

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<212>  DNA
<213>  Homo sapiens

<400>  274
gagaagattc aggacctctt ggtggactct ggaaagttca tctacttaga                    50


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<400> 276
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<210> 277
<211> 50
<212> DNA
<213> Homo sapiens

<400> 277
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<210> 278
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<213> Homo sapiens

<400> 278
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<213> Homo sapiens

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<400>   285
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<210>   286
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<212>   DNA
<213>   Homo sapiens

<400>   286
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<210>   287
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<213>   Homo sapiens

<400>   287
ttagggcagt ggagaatcag ggtgtatcta ataaattcct tcatggagct                50


<210>   288
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<213>   Homo sapiens

<400>   288
agctgctgac ttgactgtca tcctgttctt gttagccatt gtgaataaga                50


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<212>   DNA
<213>   Homo sapiens
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<210> 290
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<210> 291
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<213> Homo sapiens

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<210> 294
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<210> 298
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<210>  305
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<213>  Homo sapiens

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ccaatctaat ttaaaccctc ataacaggac ataagcttgc gcccgcatct              50


<210>  306
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cctggttaca ataatgaaac tgtcgtggag taaagaggga aacatgacca              50


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<212>  DNA
<213>  Homo sapiens

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<210>  309
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<213>  Homo sapiens

<400>  309
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<212>  DNA
<213>  Homo sapiens

<400>  313
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<213>  Homo sapiens

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<210> 321
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<210> 322
<211> 50
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<210> 325
<211> 50
<212> DNA
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<210> 326
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<212> DNA
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<400> 326
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<210> 329
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<210> 330
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<210>  332
<211>  50
<212>  DNA
<213>  Homo sapiens

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tggtcgctcg ctcctctccc acttggataa ctgtggtaat tctagagcta atacatgccg    180

acgggcgctg accccttcg cgggggggat gcgtgcattt atcagatcaa aaccaacccg    240

gtcagcccct ctccggcccc ggccggggg cgggcgccgg cggctttggt gactctagat    300

aacctcgggc cgatcgcacg cccccgtgg cggcgacgac ccattcgaac gtctgcccta    360

tcaactttcg atggtagtcg ccgtgcctac catggtgacc acgggtgacg gggaatcagg    420

gttcgattcc ggagagggag cctgagaaac ggctaccaca tccaaggaag gcagcaggcg    480

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ggcaagtctg gtgccagcag ccgcggtaat tccagctcca atagcgtata ttaaagttgc    660

tgcagttaaa aagctcgtag ttggatcttg ggagcgggcg gcggtccgc cgcgaggcga    720

gccaccgccc gtccccgccc cttgcctctc ggcgccccct cgatgctctt agctgagtgt    780

cccgcggggc ccgaagcgtt tactttgaaa aaattagagt gttcaaagca ggcccgagcc    840

gcctggatac cgcagctagg aataatggaa taggaccgcg gttctatttt gttggttttc    900
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ggaactgagg ccatgattaa gagggacggc cggggggcatt cgtattgcgc cgctagaggt      960

gaaattcttg gaccggcgca agacggacca gagcgaaagc atttgccaag aatgttttca     1020

ttaatcaaga acgaaagtcg gaggttcgaa gacgatcaga taccgtcgta gttccgacca     1080

taaacgatgc cgaccggcga tgcggcggcg ttattcccat gacccgccgg gcagcttccg     1140

ggaaaccaaa gtctttgggt tccggggggga gtatggttgc aaagctgaaa cttaaaggaa     1200

ttgacggaag ggcaccacca ggagtggagc ctgcggctta atttgactca acacgggaaa     1260

cctcacccgg cccggacacg gacaggattg acagattgat agctctttct cgattccgtg     1320

ggtggtggtg catggccgtt cttagttggt ggagcgattt gtctggttaa ttccgataac     1380

gaacgagact ctggcatgct aactagttac gcgacccccg agcggtcggc gtcccccaac     1440

ttcttagagg gacaagtggc gttcagccac ccgagattga gcaataacag gtctgtgatg     1500

cccttagatg tccggggctg cacgcgcgct acactgactg gctcagcgtg tgcctaccct     1560

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ttattcccca tgaacgagga attcccagta agtgcgggtc ataagcttgc gttgattaag     1680

tccctgccct ttgtacacac cgcccgtcgc tactaccgat tggatggttt agtgaggccc     1740

tcggatcggc cccgccgggg tcggcccacg gccctggcgg agcgctgaga agacggtcga     1800

acttgactat ctagaggaag taaaagtcgt aacaaggttt ccgtaggtga acctgcggaa     1860

ggatcatta                                                              1869


<210>  334
<211>  1793
<212>  DNA
<213>  Homo sapiens

<400>  334
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gtgcaaggcc ggcttcgcgg gcgacgatgc cccccgggcc gtcttcccct ccatcgtggg      180

gcgccccagg caccagggcg tgatggtggg catgggtcag aaggattcct atgtgggcga      240

cgaggcccag agcaagagag gcatcctcac cctgaagtac cccatcgagc acggcatcgt      300

caccaactgg gacgacatgg agaaaatctg gcaccacacc ttctacaatg agctgcgtgt      360

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ccaggctgtg ctatccctgt acgcctctgg ccgtaccact ggcatcgtga tggactccgg      540

tgacggggtc acccacactg tgcccatcta cgaggggtat gccctccccc atgccatcct      600
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gcgtctggac ctggctggcc gggacctgac tgactacctc atgaagatcc tcaccgagcg    660

cggctacagc ttcaccacca cggccgagcg ggaaatcgtg cgtgacatta aggagaagct    720

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ctgccctgag gcactcttcc agccttcctt cctgggcatg gagtcctgtg gcatccacga    900

aactaccttc aactccatca tgaagtgtga cgtggacatc cgcaaagacc tgtacgccaa    960

cacagtgctg tctggcggca ccaccatgta ccctggcatt gccgacagga tgcagaagga    1020

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gatcagcaag caggagtatg acgagtccgg cccctccatc gtccaccgca aatgcttcta    1200

ggcggactat gacttagttg cgttacaccc tttcttgaca aaacctaact tgcgcagaaa    1260

acaagatgag attggcatgg ctttatttgt ttttttttgtt ttgttttggt ttttttttttt    1320

tttttggctt gactcaggat ttaaaaactg gaacggtgaa ggtgacagca gtcggttgga    1380

gcgagcatcc cccaaagttc acaatgtggc cgaggacttt gattgcacat tgttgttttt    1440

ttaatagtca ttccaaatat gagatgcatt gttacaggaa gtcccttgcc atcctaaaag    1500

ccaccccact tctctctaag gagaatggcc cagtcctctc ccaagtccac acaggggagg    1560

tgatagcatt gctttcgtgt aaattatgta atgcaaaatt tttaatctt tcgccttaat    1620

actttttat tttgttttat tttgaatgat gagccttcgt gcccccccctt cccccttttt    1680

gtcccccaac ttgagatgta tgaaggcttt tggtctccct gggagtgggt ggaggcagcc    1740

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tcgggccgtt gttgtggggc tgcgcgctgg ggctgcaggg cgggatgctg tacccccagg    120

agagcccgtc gcgggagtgc aaggagctgg acggcctctg gagcttccgc gccgacttct    180

ctgacaaccg acgccggggc ttcgaggagc agtggtaccg gcggccgctg tgggagtcag    240

gccccaccgt ggacatgcca gttccctcca gcttcaatga catcagccag gactggcgtc    300

tgcggcattt tgtcggctgg gtgtggtacg aacgggaggt gatcctgccg gagcgatgga    360

cccaggacct gcgcacaaga gtggtgctga ggattggcag tgcccattcc tatgccatcg    420
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tgtgggtgaa tggggtcgac acgctagagc atgagggggg ctacctcccc ttcgaggccg     480

acatcagcaa cctggtccag gtggggcccc tgccctcccg gctccgaatc actatcgcca     540

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cctccaagta tcccaagggt tactttgtcc agaacacata ttttgacttt ttcaactacg     660

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ccgtcaccac cagcgtggag caagacagtg ggctggtgaa ttaccagatc tctgtcaagg     780

gcagtaacct gttcaagttg gaagtgcgtc ttttggatgc agaaaacaaa gtcgtggcga     840

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cactggggcc tgtgtctgac ttctacacac tccctgtggg gatccgcact gtggctgtca    1020

ccaagagcca gttcctcatc aatgggaaac ctttctattt ccacggtgtc aacaagcatg    1080

aggatgcgga catccgaggg aagggcttcg actggccgct gctggtgaag gacttcaacc    1140

tgcttcgctg gcttggtgcc aacgctttcc gtaccagcca ctaccctat gcagaggaag    1200

tgatgcagat gtgtgaccgc tatgggattg tggtcatcga tgagtgtccc ggcgtgggcc    1260

tggcgctgcc gcagttcttc aacaacgttt ctctgcatca ccacatgcag gtgatggaag    1320

aagtggtgcg tagggacaag aaccaccccg cggtcgtgat gtggtctgtg gccaacgagc    1380

ctgcgtccca cctagaatct gctggctact acttgaagat ggtgatcgct cacaccaaat    1440

ccttggaccc ctcccggcct gtgacctttg tgagcaactc taactatgca gcagacaagg    1500

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tcatgactga acagtcaccg acgagagtgc tggggaataa aaaggggatc ttcactcggc    1860

agagacaacc aaaaagtgca gcgttccttt tgcgagagag atactggaag attgccaatg    1920

aaaccaggta tcccactca gtagccaagt cacaatgttt ggaaaacagc ccgtttactt    1980

gagcaagact gataccacct gcgtgtccct tcctccccga gtcagggcga cttccacagc    2040

agcagaacaa gtgcctcctg gactgttcac ggcagaccag aacgtttctg gcctgggttt    2100

tgtggtcatc tattctagca gggaacacta aaggtggaaa taaaagattt tctattatgg    2160

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<212>   DNA
<213>   Homo sapiens

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ggattattgg aaatttgtta taatgaatga aacattttgt catataagat tcatatttac     840

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ggaaatcaga aaagttgtac agagtttaga acaaacagct cgagagattt taactctact     360

gcaaggggtc catcagggtg ctgggtttca ggacattcca aagaggtgtt tgaaagctcg     420

agaacatttt ggtacagtaa aaacacatct aacatctttg aagaccaaat ttcctgctga     480
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tcttggcatt gagccagatc gggagaaagg atttcatctg gatgtagaag attatctctc      660

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55

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<212> DNA
<213> Homo sapiens

<400> 339

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tgggtctcag tcctccactt cccgtgtcct ctggaagttg tcaggagcaa tgttgcgctt     240

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gcctgtagcc ctgaggtgcc cccaggtgcc ctactggttg tgggcctctg tcagcccccg     420

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<211> 1363
<212> DNA
<213> Homo sapiens

<400> 340

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58

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tctctcagca tcccctctag ctccttacac cctagcgggg cccctcaact ccccaacccc    360

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gatgggattg aaggggcttc taatgaccca gatatggaaa cagaagacaa aattgtaagc    1320

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<212>  DNA
<213>  Homo sapiens

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caaggtggtt aagactcacc agttcctgtt tggtattgga cgctgtccca tcctggctac    180

ccaaggacca aactgttctc aaatccacct taaggcaaca aaggctggag gagattctcc    240

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gattgtgcag aaggcagccc cagaagtcca ggaagatgtg aaggctttca agacagatct    360
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ccgacaccct caggtcttgc aagccacaca ggagaccctg cagcgtcatg gtgctggagc    720

tggtggcacc cgcaacatct caggcaccag taagtttcat gtggagcttg agcaggagct    780

ggctgagctg caccagaagg actcagccct gctcttctcc tcctgctttg ttgccaatga    840

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caccacctat gcctgagaag ccagctgcct aggattcaca ccccacctgc gcttcacttg   1860

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<211>  2673
<212>  DNA
<213>  Homo sapiens
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60

<400> 342

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61

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<213> Homo sapiens

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gaaactaaat ccacaacctt tggagaccca ggaacaccct ccaatctctg tgtgttttgt    240

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taagcatctg aagccatggg ccacacacgg aggcaggaa catcaccatc caagtgtcca    420

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atgatgtctg gggacatgaa tatatggccc gagtacaaga accggaccat ctttgatatc    660

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caaatctcag gtgtccgagg aagaaggcaa agaagtagag tcagataaag aaaaaggtga      420

aggaggtcag aaagagatag aatttggaac cagtcttgat gaagagatca ttttaaaggc      480

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tttctgaagc atgtgaatat tatctcgatc gttaaaagtc ctgctcagga agaactcaga      660

gaagatccag attctgaaat taaggaagga gaaggacttg aagagtgctc caaaatagaa      720

gtaaaagaag aaagccctca atcaaaagca gaaacagaat taaaagcttc ccaaaaacca      780
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64

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66

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69

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<210> 361
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<212> DNA
<213> Homo sapiens

<400> 361
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<210> 362
<211> 1498
<212> DNA
<213> Homo sapiens

<400> 362
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<210> 363
<211> 3334
<212> DNA
<213> Homo sapiens

<400> 363
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tgctcaccat cctggtcctg gccatgtgga aggtcggctt cttcaagcgg aaccggccac    3120

ccctggaaga agatgatgaa gaggggggagt gatggtgcag cctacactat tctagcagga    3180
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96

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aaacacagga gctgggccgt gactacagga cctgtctgac gatagtccaa aaactgaaga    360

agatggtgga taagcccacc cagagaagtg tttccaatgc tgcgacccgg gtgtgtagga    420

cggggaggtc acgatggcgc gacgtctgca gaaatttcat gaggaggtat cagtctagag    480

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cagaatccac tctccagtct ccctcccctg actccctctg ctgtcctccc ctctcacgag    720

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<212>   DNA
<213>   Homo sapiens

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aagagccaac aaaacagata atgcttgtta agaaagagtt tccctatcca tgctatgacc    360

cagccacacg cgaaggtgac cttaaacttt tacagctgac ggaaaaagca aaaattaaca    420

aatatgtgac tatccttcat ctacctaaaa aggggggatga tgtgaaacca ggaaccatgt    480
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accctgtgat tggaatgaat atggtttgtg ctggaagcct ccgaggtgga agagactcgt        660

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ttggccttga aaataaatgc ggagaccctc gtgggcctgg tgtctatatt cttctctcaa        780

agaaacacct caactggata attatgacta tcaagggagc agtttaaata accgtttcct        840

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<211>   576
<212>   DNA
<213>   Homo sapiens

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ggccctggag aggatgttcc tgtccttccc caccaccaag acctacttcc cgcacttcga        180

cctgagccac ggctctgccc aggttaaggg ccacggcaag aaggtggccg acgcgctgac        240

caacgccgtg gcgcacgtgg acgacatgcc caacgcgctg tccgccctga gcgacctgca        300

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<211>   589
<212>   DNA
<213>   Homo sapiens

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caagctgagc gagctgcacg cctacatcct gcgcgtggac ccggtcaact tcaagctcct        360
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gtcccactgc ctgctggtca ccctggccgc gcgcttcccc gccgacttca cggccgaggc        420

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<211>   626
<212>   DNA
<213>   Homo sapiens

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gcacctttgc cacactgagt gagctgcact gtgacaagct gcacgtggat cctgagaact        360

tcaggctcct gggcaacgtg ctggtctgtg tgctggccca tcactttggc aaagaattca        420

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taataaaaaa catttatttt cattgc                                            626
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<212>   DNA
<213>   Homo sapiens

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tcaggctctt gggcaatgtg ctggtgtgtg tgctggcccg caactttggc aaggaattca        420

ccccacaaat gcaggctgcc tatcagaagg tggtggctgg tgtggctaat gccctggctc        480

acaagtacca ttgagatcct ggactgtttc ctgataacca taagaagacc ctatttccct        540
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agattctatt ttctgaactt gggaacacaa tgcctacttc aagggtatgg cttctgccta    600

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<210> 370
<211> 816
<212> DNA
<213> Homo sapiens

<400> 370
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gacttttaag taccatggag aacagggggc cagaacttcg gcagtaaaga ataaaaggcc    180

agacagagag gcagcagcac atatctgctt ccgacacagc tgcaatcact agcaagctct    240

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tcctgtgacc ctgacaccct ccttctgcac atggggactg ggcttggcct tgagagaaag    780

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<210> 371
<211> 584
<212> DNA
<213> Homo sapiens

<400> 371
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atgctggagg agaaaccctg ggaaggctcc tggttgtcta cccatggacc cagaggttct    180

ttgacagctt tggcaacctg tcctctgcct ctgccatcat gggcaacccc aaagtcaagg    240

cacatggcaa gaaggtgctg acttccttgg agatgccac aaagcacctg atgatctca      300

agggcacctt tgcccagctg agtgaactgc actgtgacaa gctgcatgtg gatcctgaga    360

acttcaagct cctgggaaat gtgctggtga ccgttttggc aatccatttc ggcaaagaat    420
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tcacccctga ggtgcaggct tcctggcaga agatggtgac tgcagtggcc agtgccctgt    480

cctccagata ccactgagct cactgcccat gattcagagc tttcaaggat aggctttatt    540

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<213>   Homo sapiens

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cgtggagcgc ctggacgacc tacccacgc gctgtccgcg ctgagccacc tgcacgcgtg    420

ccagctgcga gtggacccgg ccagcttcca gctcctgggc cactgcctgc tggtaaccct    480

cgcccggcac taccccggag acttcagccc cgcgctgcag gcgtcgctgg acaagttcct    540

gagccacgtt atctcggcgc tggtttccga gtaccgctga actgtgggtg ggtggccgcg    600

ggatccccag gcgaccttcc ccgtgtttga gtaaagcctc tcccaggagc a             651
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<211>   1157
<212>   DNA
<213>   Homo sapiens

<400>   373
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ggccatcaag gcggaccatg tgtcaactta tgccgcgttt gtacagacgc atagaccaac    180

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cactcaggcc accaacgatc cccctgaggt gaccgtgttt cccaaggagc tgtggagct    420

gggccagccc aacaccctca tctgccacat tgacaagttc ttcccaccag tgctcaacgt    480

cacgtggctg tgcaacgggg agctggtcac tgagggtgtc gctgagagcc tcttcctgcc    540

cagaacagat tacagcttcc acaagttcca ttacctgacc tttgtgccct cagcagagga    600
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cttctatgac tgcagggtgg agcactgggg cttggaccag ccgctcctca agcactggga    660

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ggtgctgggc ctagtcggca tcatcgtggg caccgtcctc atcataaagt ctctgcgttc    780

tggccatgac ccccgggccc aggggaccct gtgaaatact gtaaaggtga caaaatatct    840

gaacagaaga ggacttagga gagatctgaa ctccagctgc cctacaaact ccatctcagc    900

ttttcttctc acttcatgtg aaaactactc cagtggctga ctgaattgct gacccttcaa    960

gctctgtcct tatccattac ctcaaagcag tcattcctta gtaaagtttc caacaaatag   1020

aaattaatga cactttggta gcactaatat ggagattatc ctttcattga gcctttatc   1080

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aaatacttca gtatttc                                                  1157
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<211>  1096
<212>  DNA
<213>  Homo sapiens

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ttttacggtc cctctggcca gtacacccat gaatttgatg gagatgagca gttctacgtg    180

gacctggaga ggaaggagac tgcctggcgg tggcctgagt tcagcaaatt tggaggtttt    240

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aaattccttt tatgag                                                      1096
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<211>   1182
<212>   DNA
<213>   Homo sapiens

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tggtgctgag ctccccactg gctttggctg gggacacccg accacgtttc ttgtggcagc     180

ttaagtttga atgtcatttc ttcaatggga cggagcgggt gcggttgctg gaaagatgca     240

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tgcagcggcg agttgagcct aaggtgactg tgtatccttc aaagacccag cccctgcagc     480

accacaacct cctggtctgc tctgtgagtg gtttctatcc aggcagcatt gaagtcaggt     540

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acacctgcca agtggagcac ccaagtgtga cgagccctct cacagtggaa tggagagcac     720

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ttctcaggac ctggttgcta ctggttcggc aactgcagaa aatgtcctcc cttgtggctt    1020

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tttgtgctcc cctttgccta aaccgtatgg cctcccgtgc atctgtactc accctgtacg    1140

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<211>   2610
<212>   DNA
<213>   Homo sapiens

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aatgcagttg ctgaaagggg ggcaaatact ctgcgatctc actaagacaa aaggaagtgg   240

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ctcttttttt ctatacaact tggaccattc tcatgccaac tattacttct gcaacctatc   360

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gccagttttc ctcaacttga agtgcaagat tctcttattt ccgggaccac ggagagtctg   720

acttaactac atacatcttc tgctggtgtt ttgttcaatc tggaagaatg actgtatcag   780

tcaatgggga ttttaacaga ctgccttggt actgccgagt cctctcaaaa caaacaccct   840

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taatcagtca agggagatgc ttcaaagctg gagctatttt atttctgaga tgttgatgtg  1140

aactgtacat tagtacatac tcagtactct ccttcaattg ctgaacccca gttgaccatt  1200

ttaccaagac tttagatgct ttcttgtgcc ctcaattttc tttttaaaaa tacttctaca  1260

tgactgcttg acagcccaac agccactctc aatagagagc tatgtcttac attctttcct  1320

ctgctgctca atagttttat atatctatgc atacatatat acacacatat gtatataaaa  1380

ttcataatga atatatttgc ctatattctc cctacaagaa tatttttgct ccagaaagac  1440

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aaaatcatct ttaatgggcc agcattctca tggggtagag cagaatattc atttagcctg  1680

aaagctgcag ttactatagg ttgctgtcag actatacccca tggtgcctct gggcttgaca  1740

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cctgggaatc acagtggtct acctgcattc ataattccag gatctgtgaa gagcacatat  1920
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cagccaatgt cgatgcaaca acatttgtaa ctttaggtaa actgggatta tgttgtagtt    2160

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ttttaagagg agccacttat caaagagatt ttaacagtag taagaaggca aagaataaac    2580

atttgatatt cagcaactga aaaaaaaaaa                                     2610
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<212>  DNA
<213>  Homo sapiens

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gccacctgct gcagtctaca cagcttcggg aagaggaaag gaacctcaga ccttccagat     180

cgcttcctct cgcaacaaac tatttgtcgc aggaataaag atggctgctg aaccagtaga     240

agacaattgc atcaactttg tggcaatgaa atttattgac aatacgcttt actttatagc     300

tgaagatgat gaaaacctgg aatcagatta ctttggcaag cttgaatcta aattatcagt     360

cataagaaat ttgaatgacc aagttctctt cattgaccaa ggaaatcggc ctctatttga     420

agatatgact gattctgact gtagagataa tgcaccccgg accatattta ttataagtat     480

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cactgttcaa aacgaagact agctattaaa atttcatgcc gggcgcagtg gctcacgcct     840

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ccagcctgac caacatggtg aaacctcatc tctactaaaa atacaaaaaa ttagctgagt   960

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actccggagg tagaggttgt ggtgagccga gattgcacca ttgcgctcta gcctgggcaa   1080

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atgtg   1145

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<213>   Homo sapiens

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cccagacaac gcccttgaag acaagctggg ttaactgctc taacatgatc gatgaaatta   180

taacacactt aaagcagcca cctttgcctt tgctggactt caacaacctc aatggggaag   240

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ctacaaataa atacaaggct tttttagaca aacaaaatca agtaaaattt ggaagttatt   1920

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116

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cccaaccttc aaagttcaag tagtgatatg gatgactcca cagaaaggga gcagtcacgc     300

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acca                                                                 1204


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tgcaccaaag tctcaagctt tgtacactgg ataaagaaaa ccatgaaacg ctactaacta    780

caggaagcaa actaagcccc cgctgtaatg aaacaccttc tctggagcca agtccagatt    840

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<212>   DNA
<213>   Homo sapiens
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<213> Homo sapiens

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cttcctgaag acctgaacac cgctcccata aagccatggc ttgccttgga tttcagcggc   180

acaaggctca gctgaacctg gctaccagga cctggccctg cactctcctg ttttttcttc   240

155

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tccgggtgac agtgcttcgg caggctgaca gccaggtgac tgaagtctgt gcggcaacct    420

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acatgtggtt aatgccatgg acagaagaag gcagcaggtg gcagaatggg gtgcatgaag   1860

gtttctgaaa attaacactg cttgtgtttt taactcaata ttttccatga aaatgcaaca   1920

acatgtataa tatttttaat taaataaaaa tctgtggtgg tcgttttaaa aaaaaaaaa   1980

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<213>   Homo sapiens

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cgagccagtt  ccgggtgtcg  ccgctggatc  ggacctggaa  cctgggcgag  acagtggagc     240

tgaagtgcca  ggtgctgctg  tccaacccga  cgtcgggctg  ctcgtggctc  ttccagccgc     300

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gtgggaaaga  ttactttttc  tttatgtgtt  tgacgggaaa  caaaactagg  taaaatctac    1020

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157

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caactagcag atacagggat gaggcagacc tgactctctt aaggaggctg agagcccaaa   1860

ctgctgtccc aaacatgcac ttccttgctt aaggtatggt acaagcaatg cctgcccatt   1920

ggagagaaaa aacttaagta gataaggaaa taagaaccac tcataattct tcaccttagg   1980

aataatctcc tgttaatatg gtgtacattc ttcctgatta ttttctacac atacatgtaa   2040

aatatgtctt tcttttttaa atagggttgt actatgctgt tatgagtggc tttaatgaat   2100

aaacatttgt agcatcctct ttaatgggta aacagcaaaa aaaaaaaaaa aaaaaaaaaa   2160

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<212>   DNA
<213>   Homo sapiens
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ctcttgagta gctgggactt caggagactg aagccaagga taccagcaga gccaacattt    180

gcttcaagtt cctgggcctg ctgacagcgt gcaggatgct gttggaaccc ggcagaggct    240

gctgtgccct ggccatcctg ctggcaattg tggacatcca gtctggtgga tgcattaaca    300

tcaccagctc agcttcccag gaaggaacgc gactaaactt aatctgtact gtatggcata    360

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ctcctgagac cagtttaaaa cagctgagac ttaaaaggga tcctgggata gatggtgttg    480

gtgaaatatc atctcagttg atgttcacca taagccaagt cacaccgttg cacagtggga    540

cctaccagtg ttgtgccaga agccagaagt caggtatccg ccttcagggc cattttttct    600

ccattctatt cacagagaca gggaactaca cagtgacggg attgaaacaa agacaacacc    660

ttgagttcag ccataatgaa ggcactctca gttcaggctt cctacaagaa aaggtctggg    720

taatgctggt caccagcctt gtggcccttc aagctttgta agcctgtcca aaagaacttt    780

taaaacagct acagcaagat gagtctgact atggcttagt atctttctca ttacaatagg    840

cacagagaag aatgcaacag ggcacagggg aagagatgct aaatatacca agaatctgtg    900

gaaatataag ctggggcaaa tcagtgtaat ccttgacttt gctcctcacc atcagggcaa    960

acttgccttc ttccctccta agctccagta aataaacaga acagctttca ccaaagtggg   1020
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ctccctcttc atcaacatag taaaataagt caaacaaaat gagaacacca aattttgggg    1140

gaataaattt ttatttaaca ctgcaaagga aagagagaga aaacaagcaa agataggtag    1200

dacagaaagg aagacagcca gatccagtga ttgacttggc atgaaaatga gaaaatgcag    1260

acagacctca acattcaaca ttcaacaaca tccatacagc actgctggag gaagaggaag    1320

atttgtgcag accaagagca ccacagacta caactgccca gcttcatcta aatacttgtt    1380

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<213> Homo sapiens

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acttaagagt tatacaagaa aatggtaggg gacgaggagg ttgtataaag gggaaaaaac    180

aacaactgca aaaagcccaa gagcctgaat ttagaccaat ctatcatctt cctcctctta    240

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<210> 418
<211> 626
<212> DNA
<213> Homo sapiens

<400> 418
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gcacctttgc cacactgagt gagctgcact gtgacaagct gcacgtggat cctgagaact    360

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<211>   1764
<212>   DNA
<213>   Homo sapiens

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aggcactatt ctaatcagta gttcacttta atatttaata agattttctg ggataacagt    1380

aagggatatt agataatata ccgtatgtat ttattactag tcttttcctc taggaaaagg    1440

gatactttga taattaaggc cagaggccca ttagttgaga aagtcacaga tatatttctc    1500

caagaaagcc aacaaccacc accacaatga cagaaatgac aacaaggccc tttaacttgt    1560

cttctagttt agagacatcc ttcatttgac atttagtaga attcctcttt ggccacaaga    1620
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<213>    Homo sapiens
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tggaaggaaa ctggcccagc agatcaagca ggaagtgcgg caggaggtag aagagtgggt       240

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tcactcctat gtcctcaaca aaaccagggc agctgcagtt gtgggaatca acagtgagac       360

aattatgaaa ccagcttcaa tttcagagga agaattgttg aatttaatca ataaactgaa       420

taatgatgat aatgtagatg gcctccttgt tcagttgcct cttccagagc atattgatga       480

gagaaggatc tgcaatgctg tttctccaga caaggatgtt gatggctttc atgtaattaa       540

tgtaggacga atgtgtttgg atcagtattc catgttaccg gctactccat ggggtgtgtg       600

ggaaataatc aagcgaactg gcattccaac cctagggaag aatgtggttg tggctggaag       660

gtcaaaaaac gttggaatgc ccattgcaat gttactgcac acagatgggg cgcatgaacg       720

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cctattttttg aaaaacaaac ttggcttgat aatcatttgg gcagcttggg taagtacgca   1980

acttactttt ccaccaaaga actgtcagca gctgcctgct tttctgtgat gtatgtatcc    2040

tgttgacttt tccagaaatt ttttaagagt ttgagttact attgaattta atcagacttt    2100

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<210> 421
<211> 2960
<212> DNA
<213> Homo sapiens

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tatctagtga gcaggcggcc gctttcgatt tcgctttccc ctaaatggct gagcttctcg    180

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cagccgccag tagggagga ctcggcggta cccggagctt caggccccac cggggcgcgg     300

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171

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gaaaaaaata aaaattattc cgtgcaaaaa aaaaaaaaaa aaaaaaaaa aaaaaaa       3478
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<210>   427
<211>   584
<212>   DNA
<213>   Homo sapiens

<400>   427
atttggccct cgaggccaag aattcggcac gaggcgctca gtttcagcag ccagataatg     60

gctatattta tctaacatct tgagttcaaa agcatgacgg cgcattttgg ggcactgaac    120

aacatcaatg caggcgtcca agtagatgca acctttcgat tcttttgaat ttttctcatc    180

tttataggaa ttgagaatat atgaaccgtc aggaagttgg gtcaagtaaa aatatcgtct    240

cttgaatacc ttcatggtta ctgtgatggt actatttaca tttgctttat gcaaccagcc    300

ttgttttatc acaccaccct tctgagaaca taaagaagat gagtcctcat ctttctcaca    360

gtcttcatct atctcaaata catgattagg aatcttttct ggtctcaaag atttacatgg    420

caacattcga aagtccccag agaagtcctc atacttgtag tttaccacgt gccaatctgt    480

gctataggtt ttaatacact ctttaacaaa taaactctgg gccctctttt cagcatcttc    540

tggtacagta aaactgaacc gttctgggtt gacgacctat aacc                     584
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<210>   428
<211>   1679
<212>   DNA
<213>   Homo sapiens

<400>   428
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caccgcatct ggagaaccag cggttaccat ggaggggatc agtatataca cttcagataa    120

ctacaccgag gaaatgggct caggggacta tgactccatg aaggaaccct gttccgtga     180

agaaaatgct aatttcaata aaatcttcct gcccaccatc tactccatca tcttcttaac    240

tggcattgtg ggcaatggat tggtcatcct ggtcatgggt taccagaaga aactgagaag    300

catgacggac aagtacaggc tgcacctgtc agtggccgac ctcctctttg tcatcacgct    360

tcccttctgg gcagttgatg ccgtggcaaa ctggtacttt gggaacttcc tatgcaaggc    420

agtccatgtc atctacacag tcaacctcta cagcagtgtc ctcatcctgg ccttcatcag    480
```

```
tctggaccgc tacctggcca tcgtccacgc caccaacagt cagaggccaa ggaagctgtt    540

ggctgaaaag gtggtctatg ttggcgtctg datccctgcc ctcctgctga ctattcccga    600

cttcatcttt gccaacgtca gtgaggcaga tgacagatat atctgtgacc gcttctaccc    660

caatgacttg tgggtggttg tgttccagtt tcagcacatc atggttggcc ttatcctgcc    720

tggtattgtc atcctgtcct gctattgcat tatcatctcc aagctgtcac actccaaggg    780

ccaccagaag cgcaaggccc tcaagaccac agtcatcctc atcctggctt tcttcgcctg    840

ttggctgcct tactacattg ggatcagcat cgactccttc atcctcctgg aaatcatcaa    900

gcaagggtgt gagtttgaga acactgtgca caagtggatt tccatcaccg aggccctagc    960

tttcttccac tgttgtctga accccatcct ctatgctttc cttggagcca aatttaaaac   1020

ctctgcccag cacgcactca cctctgtgag cagagggtcc agcctcaaga tcctctccaa   1080

aggaaagcga ggtggacatt catctgtttc cactgagtct gagtcttcaa gttttcactc   1140

cagctaacac agatgtaaaa gacttttttt tatacgataa ataacttttt tttaagttac   1200

acatttttca gatataaaag actgaccaat attgtacagt ttttattgct tgttggattt   1260

ttgtcttgtg tttctttagt ttttgtgaag tttaattgac ttatttatat aaattttttt   1320

tgtttcatat tgatgtgtgt ctaggcagga cctgtggcca agttcttagt tgctgtatgt   1380

ctcgtggtag gactgtagaa aagggaactg aacattccag agcgtgtagt gaatcacgta   1440

aagctagaaa tgatccccag ctgtttatgc atagataatc tctccattcc cgtggaacgt   1500

ttttcctgtt cttaagacgt gattttgctg tagaagatgg cacttataac caaagcccaa   1560

agtggtatag aaatgctggt ttttcagttt tcaggagtgg gttgatttca gcacctacag   1620

tgtacagtct tgtattaagt tgttaataaa agtacatgtt aaacttactt agtgttatg    1679
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<210>   429
<211>   1702
<212>   DNA
<213>   Homo sapiens

<400>   429
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tagggaatct tgagaataaa gatgagctct gaaaattgtt tcgtagcaga gaacagctct    120

ttgcatccgg agagtggaca agaaaatgat gccaccagtc cccatttctc aacacgtcat    180

gaagggtcct tccaagttcc tgtcctgtgt gctgtaatga atgtggtctt catcaccatt    240

ttaatcatag ctctcattgc cttatcagtg ggccaataca attgtccagg ccaatacaca    300

ttctcaatgc catcagacag ccatgtttct tcatgctctg aggactgggt tggctaccag    360

aggaaatgct actttatttc tactgtgaag aggagctgga cttcagccca aaatgcttgt    420
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173

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tctgaacatg gtgctactct tgctgtcatt gattctgaaa aggacatgaa ctttctaaaa      480

cgatacgcag gtagagagga acactgggtt ggactgaaaa aggaacctgg tcacccatgg      540

aagtggtcaa atggcaaaga atttaacaac tggttcaacg ttacagggtc tgacaagtgt      600

gtttttctga aaacacaga ggtcagcagc atggaatgtg agaagaattt atactggata      660

tgtaacaaac cttacaaata ataaggaaac atgttcactt attgactatt atagaatgga      720

actcaaggaa atctgtgtca gtggatgctg ctctgtggtc cgaagtcttc catagagact      780

ttgtgaaaaa aaatttttata gtgtcttggg aattttcttc caaacagaac tatggaaaaa      840

aaggaagaaa ttccaggaaa atctgcactg tgggctttta ttgccatgag ctagaagcat      900

cacaggttga ccaataacca tgcccaagaa tgagaagaat gactatgcaa cctttggatg      960

cactttatat tattttgaat ccagaaataa tgaaataact aggcgtggac ttactattta     1020

ttgctgaatg actaccaaca gtgagagccc ttcatgcatt tgcactactg gaaggagtta     1080

gatgttggta ctagatactg aatgtaaaca aaggaattat ggctggtaac ataggttttt     1140

agtctaattg aatcccttaa actcagggag catttataaa tggacaaatg cttatgaaac     1200

taagatttgt aatatttctc tcttttttaga gaaatttgcc aatttacttt gttattttc      1260

cccaaaaaga atgggatgat cgtgtattta ttttttttact tcctcagctg tagacaggtc     1320

cttttcgatg gtacatattt ctttgccttt ataatctttt atacagtgtc ttacagagaa     1380

aagacataag caaagactat gaggaatatt tgcaagacat agaatagtgt tggaaaatgt     1440

gcaatatgtg atgtggcaaa tctctattag gaaatattct gtaatcttca gacctagaat     1500

aatactagtc ttataatagg tttgtgactt tcctaaatca attctattac gtgcaatact     1560

tcaatacttc atttaaaata ttttttatgtg caataaaatg tatttgtttg tattttgtgt     1620

tcagtacaat tataagctgt ttttatatat gtgaaataaa agtagaataa acacaaaaaa     1680

aaaaaaaaaa aaaaaaaaaa aa                                                1702
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<210> 430
<211> 1237
<212> DNA
<213> Homo sapiens

<400> 430

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gctgcagagg attcctgcag aggatcaaga cagcacgtgg acctcgcaca gcctctccca       60

caggtaccat gaaggtctcc gcggcagccc tcgctgtcat cctcattgct actgccctct      120

gcgctcctgc atctgcctcc ccatattcct cggacaccac accctgctgc tttgcctaca      180

ttgcccgccc actgccccgt gcccacatca aggagtattt ctacaccagt ggcaagtgct      240

ccaacccagc agtcgtcttt gtcacccgaa agaaccgcca agtgtgtgcc aacccagaga      300
```

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agaaatgggt tcgggagtac atcaactctt tggagatgag ctaggatgga gagtccttga    360

acctgaactt acacaaattt gcctgtttct gcttgctctt gtcctagctt gggaggcttc    420

ccctcactat cctaccccac ccgctccttg aagggcccag attctaccac acagcagcag    480

ttacaaaaac cttccccagg ctggacgtgg tggctcacgc ctgtaatccc agcactttgg    540

gaggccaagg tgggtggatc acttgaggtc aggagttcga gaccagcctg gccaacatga    600

tgaaacccca tctctactaa aaatacaaaa aattagccgg gcgtggtagc gggcgcctgt    660

agtcccagct actcgggagg ctgaggcagg agaatggcgt gaacccggga ggcggagctt    720

gcagtgagcc gagatcgcgc cactgcactc cagcctgggc gacagagcga gactccgtct    780

caaaaaaaaa aaaaaaaaaa aaaatacaaa aattagccgg gcgtggtggc ccacgcctgt    840

aatcccagct actcgggagg ctaaggcagg aaaattgttt gaacccagga ggtggaggct    900

gcagtgagct gagattgtgc cacttcactc cagcctgggt gacaaagtga gactccgtca    960

caacaacaac aacaaaaagc ttccccaact aaagcctaga agagcttctg aggcgctgct   1020

ttgtcaaaag gaagtctcta ggttctgagc tctggctttg ccttggcttt gccagggctc   1080

tgtgaccagg aaggaagtca gcatgcctct agaggcaagg aggggaggaa cactgcactc   1140

ttaagcttcc gccgtctcaa cccctcacag gagcttactg gcaaacatga aaaatcggct   1200

taccattaaa gttctcaatg caaccataaa aaaaaa                            1237
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<210> 431
<211> 1125
<212> DNA
<213> Homo sapiens

<400> 431
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ttctgccctc gagcccaccg ggaacgaaag agaagctcta tctcgcctcc aggagcccag     60

ctatgaactc cttctccaca agcgccttcg gtccagttgc cttctccctg gggctgctcc    120

tggtgttgcc tgctgccttc cctgccccag tacccccagg agaagattcc aaagatgtag    180

ccgccccaca cagacagcca ctcacctctt cagaacgaat tgacaaacaa attcggtaca    240

tcctcgacgg catctcagcc ctgagaaagg agacatgtaa caagagtaac atgtgtgaaa    300

gcagcaaaga ggcactggca gaaaacaacc tgaaccttcc aaagatggct gaaaaagatg    360

gatgcttcca atctggattc aatgaggaga cttgcctggt gaaaatcatc actggtcttt    420

tggagtttga ggtatcccta gagtacctcc agaacagatt tgagtagt gaggaacaag    480

ccagagctgt gcagatgagt acaaagtcc tgatccagtt cctgcagaaa aaggcaaaga    540

atctagatgc aataaccacc cctgacccaa ccacaaatgc cagcctgctg acgaagctgc    600

aggcacagaa ccagtggctg caggacatga caactcatct cattctgcgc agctttaagg    660
```

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agttcctgca gtccagcctg agggctcttc ggcaaatgta gcatgggcac ctcagattgt      720

tgttgttaat gggcattcct tcttctggtc agaaacctgt ccactgggca cagaacttat      780

gttgttctct atggagaact aaaagtatga gcgttaggac actattttaa ttatttttaa      840

tttattaata tttaaatatg tgaagctgag ttaatttatg taagtcatat ttatattttt      900

aagaagtacc acttgaaaca ttttatgtat tagtttttgaa ataataatgg aaagtggcta      960

tgcagtttga atatcctttg tttcagagcc agatcatttc ttggaaagtg taggcttacc     1020

tcaaataaat ggctaactta tacatatttt taaagaaata tttatattgt atttatataa     1080

tgtataaatg gtttttatac caataaatgg cattttaaaa aattc                      1125
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<210>   432
<211>   1047
<212>   DNA
<213>   Homo sapiens

<400>   432
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attcagtcag tctttggggg tttaaagaaa ttccaaagag tcatcagaag aggaaaaatg      120

aaggtaatgt tttttcagac aggtaaagtc tttgaaaata tgtgtaatat gtaaaacatt      180

ttgacacccc cataatattt ttccagaatt aacagtataa attgcatctc ttgttcaaga      240

gttccctatc actctcttta atcactactc acagtaacct caactcctgc cacaatgtac      300

aggatgcaac tcctgtcttg cattgcacta agtcttgcac ttgtcacaaa cagtgcacct      360

acttcaagtt ctacaaagaa aacacagcta caactggagc atttactgct ggatttacag      420

atgatttga atggaattaa taattacaag aatcccaaac tcaccaggat gctcacattt      480

aagttttaca tgcccaagaa ggccacagaa ctgaaacatc ttcagtgtct agaagaagaa      540

ctcaaacctc tggaggaagt gctaaattta gctcaaagca aaaactttca cttaagaccc      600

agggacttaa tcagcaatat caacgtaata gttctggaac taaagggatc tgaaacaaca      660

ttcatgtgtg aatatgctga tgagacagca accattgtag aatttctgaa cagatggatt      720

accttttgtc aaagcatcat ctcaacactg acttgataat taagtgcttc ccacttaaaa      780

catatcaggc cttctattta tttaaatatt taaattttat atttattgtt gaatgtatgg      840

tttgctacct attgtaacta ttattcttaa tcttaaaact ataaatatgg atcttttatg      900

attctttttg taagccctag gggctctaaa atggtttcac ttatttatcc caaaatattt      960

attattatgt tgaatgttaa atatagtatc tatgtagatt ggttagtaaa actatttaat     1020

aaatttgata aatataaaaa aaaaaaa                                         1047
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<210>   433
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<211>  1242
<212>  DNA
<213>  Homo sapiens

<400>  433
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gaagatgcaa gatgaagaaa gatacatgac attgaatgta cagtcaaaga aaaggagttc   120

tgcccaaaca tctcaactta catttaaaga ttattcagtg acgttgcact ggtataaaat   180

cttactggga atatctggaa ccgtgaatgg tattctcact ttgactttga tctccttgat   240

cctgttggtt tctcagggag tattgctaaa atgccaaaaa ggaagttgtt caaatgccac   300

tcagtatgag gacactggag atctaaaagt gaataatggc acaagaagaa atataagtaa   360

taaggacctt tgtgcttcga gatctgcaga ccagacagta ctatgccaat cagaatggct   420

caaataccaa gggaagtgtt attggttctc taatgagatg aaaagctgga gtgacagtta   480

tgtgtattgt ttggaaagaa aatctcatct actaatcata catgaccaac ttgaaatggc   540

ttttatacag aaaaacctaa gacaattaaa ctacgtatgg attgggctta actttacctc   600

cttgaaaatg acatggactt gggtggatgg ttctccaata gattcaaaga tattcttcat   660

aaagggacca gctaaagaaa acagctgtgc tgccattaag gaaagcaaaa ttttctctga   720

aacctgcagc agtgttttca aatggatttg tcagtattag agtttgacaa aattcacagt   780

gaaataatca atgatcacta ttttttggcct attagtttct aatattaatc tccaggtgta   840

agattttaaa gtgcaattaa atgccaaaat ctcttctccc ttctccctcc atcatcgaca   900

ctggtctagc ctcagagtaa cccctgttaa caaactaaaa tgtacacttc aaaatttta   960

cgtgatagta taaaccaatg tgacttcatg tgatcatatc caggattttt attcgtcgct  1020

tattttatgc caaatgtgat caaattatgc ctgtttttct gtatcttgcg ttttaaattc  1080

ttaataaggt cctaaacaaa atttcttata tttctaatgg ttgaattata atgtgggttt  1140

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tcactcagct acaataaaca tcctgaatgt tttcttaaaa aa                     1242


<210>  434
<211>  2298
<212>  DNA
<213>  Homo sapiens

<400>  434
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tccccggccg tggcgcctcc gggccagacg cgctgcagcc tccagcccgc ggcaagcggg   120

cggggcggcc gcgccacccc cggccccgcg ccagcagccc ctcgccgcgc gtccagcgtt   180

cccggccagc agcctcccca tacgcagtcc tgctggaccg ccccgtcgcg ccccccactc   240
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tgaactcaag tcaccgtgga gctccgccgc cccgaaactt tcacgcgagc gggaaatatg    300

ggatgtataa aatcaaaagg gaaagacagc ttgagtgacg atggagtaga tttgaagact    360

caaccagtac gtaatactga aagaactatt tatgtgagag atccaacgtc caataaacag    420

caaaggccag ttccagaatc tcagctttta cctggacaga ggtttcaaac taaagatcca    480

gaggaacaag gagacattgt ggtagccttg taccctatg atggcatcca cccggacgac    540

ttgtctttca agaaaggaga gaagatgaaa gtcctggagg agcatggaga atggtggaaa    600

gcaaagtccc ttttaacaaa aaaagaaggc ttcatcccca gcaactatgt ggccaaactc    660

aacaccttag aaacagaaga gtggtttttc aaggatataa ccaggaagga cgcagaaagg    720

cagcttttgg caccaggaaa tagcgctgga gctttcctta ttagagaaag tgaaacatta    780

aaaggaagct tctctctgtc tgtcagagac tttgaccctg tgcatggtga tgttattaag    840

cactacaaaa ttagaagtct ggataatggg ggctattaca tctctccacg aatcactttt    900

ccctgtatca gcgacatgat taaacattac caaaagcagg cagatggctt gtgcagaaga    960

ttggagaagg cttgtattag tcccaagcca cagaagccat gggataaaga tgcctgggag   1020

atcccccggg agtccatcaa gttggtgaaa aggcttggcg ctgggcagtt tggggaagtc   1080

tggatgggtt actataacaa cagtaccaag gtggctgtga aaaccctgaa gccaggaact   1140

atgtctgtgc aagccttcct ggaagaagcc aacctcatga gaccctgca gcatgacaag   1200

ctcgtgaggc tctacgctgt ggtcaccagg gaggagccca tttacatcat caccgagtac   1260

atggccaagg gcagtttgct ggatttcctg aagagcgatg aaggtggcaa agtgctgctt   1320

ccaaagctca ttgactttc tgctcagatt gcagagggaa tggcatacat cgagcggaag   1380

aactacattc accgggacct gcgagcagct aatgttctgg tctccgagtc actaatgtgc   1440

aaaattgcag attttggcct tgctagagta attgaagata atgagtacac agcaagggaa   1500

ggtgctaagt tccctattaa gtggacggct ccagaagcaa tcaactttgg atgtttcact   1560

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atgccccgtg tggagaactg cccagatgag ctctatgaca ttatgaaaat gtgctggaaa   1740

gaaaaggcag aagagagacc aacgtttgac tacttacaga gcgtcctgga tgatttctac   1800

acagccacgg aagggcaata ccagcagcag ccttagagca cagggagacc cgtccatttg   1860

gcaggggtgg ctgcctcatt tagagaggaa aagtaaccat cactggttgc acttatgatt   1920

tcatgtgcgg ggatcatctg ccgtgcctgg atcctgaaat agaggctaaa ttactcagga   1980

agaacaccct ctaaatggga aagtattctg tactcttaga tggattctcc actcagttgc   2040
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178

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aacttggact tgtcctcagc agctggtaat cttgctctgc ttgacaacat ctgagtgcag    2100

ccgtttgaga agaaaacatc tattctctcc aaaaatgcac ccaactagct ctatgtttac    2160

aaatggacat aggactcaaa gtttcagaga ccattgcaat gaatccccaa taattgcaga    2220

actaaactca tttataaagc taaaataacc ggatatatac atagcatgac atttctttgt    2280

gctttggctt acttgttt                                                   2298
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<210> 435
<211> 2308
<212> DNA
<213> Homo sapiens

<400> 435
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gagagactgg atggacccac aagggtgaca gcccaggcgg accgatcttc ccatcccaca      60

tcctccggcg cgatgccaaa aagaggctga cggcaactgg gccttctgca gagaaagacc     120

tccgcttcac tgccccggct ggtcccaagg gtcaggaaga tggattcata cctgctgatg     180

tggggactgc tcacgttcat catggtgcct ggctgccagg cagagctctg tgacgatgac     240

ccgccagaga tcccacacgc cacattcaaa gccatggcct acaaggaagg aaccatgttg     300

aactgtgaat gcaagagagg tttccgcaga ataaaaagcg ggtcactcta tatgctctgt     360

acaggaaact ctagccactc gtcctgggac aaccaatgtc aatgcacaag ctctgccact     420

cggaacacaa cgaaacaagt gacacctcaa cctgaagaac agaaagaaag gaaaaccaca     480

gaaatgcaaa gtccaatgca gccagtggac caagcgagcc ttccaggtca ctgcagggaa     540

cctccaccat gggaaaatga agccacagag agaatttatc atttcgtggt ggggcagatg     600

gtttattatc agtgcgtcca gggatacagg gctctacaca gaggtcctgc tgagagcgtc     660

tgcaaaatga cccacgggaa gacaaggtgg acccagcccc agctcatatg cacaggtgaa     720

atggagacca gtcagtttcc aggtgaagag aagcctcagg caagccccga aggccgtcct     780

gagagtgaga cttcctgcct cgtcacaaca acagattttc aaatacagac agaaatggct     840

gcaaccatgg agacgtccat atttacaaca gagtaccagg tagcagtggc cggctgtgtt     900

ttcctgctga tcagcgtcct cctcctgagt gggctcacct ggcagcggag acagaggaag     960

agtagaagaa caatctagaa aaccaaaaga caagaattt cttggtaaga agccgggaac    1020

agacaacaga agtcatgaag cccaagtgaa atcaaaggtg ctaaatggtc gcccaggaga    1080

catccgttgt gcttgcctgc gttttggaag ctctgaagtc acatcacagg acacggggca    1140

gtggcaacct tgtctctatg ccagctcagt cccatcagag agcgagcgct acccacttct    1200

aaatagcaat ttcgccgttg aagaggaagg gcaaaaccac tagaactctc catcttattt    1260

tcatgtatat gtgttcatta aagcatgaat ggtatggaac tctctccacc ctatatgtag    1320
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tataaagaaa agtaggttta cattcatctc attccaactt cccagttcag gagtcccaag    1380

gaaagcccca gcactaacgt aaatacacaa cacacacact ctaccctata caactggaca    1440

ttgtctgcgt ggttcctttc tcagccgctt ctgactgctg attctcccgt tcacgttgcc    1500

taataaacat ccttcaagaa ctctgggctg ctacccagaa atcattttac ccttggctca    1560

atcctctaag ctaaccccct tctactgagc cttcagtctt gaatttctaa aaaacagagg    1620

ccatggcaga ataatctttg ggtaacttca aaacggggca gccaaaccca tgaggcaatg    1680

tcaggaacag aaggatgaat gaggtcccag gcagagaatc atacttagca aagtttttacc   1740

tgtgcgttac taattggcct ctttaagagt tagtttctttt gggattgcta tgaatgatac    1800

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181

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185

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186

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187

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aagccttgtc tgagatgatc cagtttttacc tggaggaggt gatgccccaa gctgagaacc      360

aagacccaga catcaaggcg catgtgaact ccctggggga gaacctgaag accctcaggc      420

tgaggctacg gcgctgtcat cgatttcttc cctgtgaaaa caagagcaag gccgtggagc      480

aggtgaagaa tgcctttaat aagctccaag agaaaggcat ctacaaagcc atgagtgagt      540

ttgacatctt catcaactac atagaagcct acatgacaat gaagatacga aactgagaca      600

tcagggtggc gactctatag actctaggac ataaattaga ggtctccaaa atcggatctg      660

gggctctggg atagctgacc cagccccttg agaaacctta ttgtacctct cttatagaat      720

atttattacc tctgatacct caacccccat ttctatttat ttactgagct tctctgtgaa      780

cgatttagaa agaagcccaa tattataatt ttttcaata tttattattt tcacctgttt      840

ttaagctgtt tccatagggt gacacactat ggtatttgag tgtttaaga taaattataa      900
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gttacataag ggaggaaaaa aaatgttctt tggggagcca acagaagctt ccattccaag      960

cctgaccacg ctttctagct gttgagctgt tttccctgac ctccctctaa tttatcttgt     1020

ctctgggctt ggggcttcct aactgctaca aatactctta ggaagagaaa ccagggagcc     1080

cctttgatga ttaattcacc ttccagtgtc tcggagggat tcccctaacc tcattcccca     1140

accacttcat tcttgaaagc tgtggccagc ttgttattta taacaaccta aatttggttc     1200

taggccgggc gcggtggctc acgcctgtaa tcccagcact ttgggaggct gaggcgggtg     1260

gatcacttga ggtcaggagt tcctaaccag cctggtcaac atggtgaaac cccgtctcta     1320

ctaaaaatac aaaaattagc cgggcatggt ggcgcgcacc tgtaatccca gctacttggg     1380

aggctgaggc aagagaattg cttgaaccca ggagatggaa gttgcagtga gctgatatca     1440

tgcccctgta ctccagcctg ggtgacagag caagactctg tctcaaaaaa taaaaataaa     1500

aataaatttg gttctaatag aactcagttt taactagaat ttattcaatt cctctgggaa     1560

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attcacatc                                                            1629
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<210> 445
<211> 1193
<212> DNA
<213> Homo sapiens

<400> 445
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acaagaacta ctgatttcaa cttctttggc ttaattctct cggaaacgat gaaatataca     120

agttatatct tggcttttca gctctgcatc gttttgggtt ctcttggctg ttactgccag     180

gacccatatg taaaagaagc agaaaacctt aagaaatatt ttaatgcagg tcattcagat     240

gtagcggata atggaactct tttcttaggc attttgaaga attggaaaga ggagagtgac     300

agaaaaataa tgcagagcca aattgtctcc ttttacttca aacttttaa aaactttaaa     360

gatgaccaga gcatccaaaa gagtgtggag accatcaagg aagacatgaa tgtcaagttt     420

ttcaatagca acaaaaagaa acgagatgac ttcgaaaagc tgactaatta ttcggtaact     480

gacttgaatg tccaacgcaa agcaatacat gaactcatcc aagtgatggc tgaactgtcg     540

ccagcagcta aaacagggaa gcgaaaaggg agtcagatgc tgtttcaagg tcgaagagca     600

tcccagtaat ggttgtcctg cctgcaatat ttgaatttta aatctaaatc tatttattaa     660

tatttaacat tatttatatg gggaatatat ttttagactc atcaatcaaa taagtattta     720

taatagcaac ttttgtgtaa tgaaaatgaa tatctattaa tatatgtatt atttataatt     780

cctatatcct gtgactgtct cacttaatcc tttgtttct gactaattag gcaaggctat      840
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gtgattacaa ggctttatct caggggccaa ctaggcagcc aacctaagca agatcccatg      900

ggttgtgtgt ttatttcact tgatgataca atgaacactt ataagtgaag tgatactatc      960

cagttactgc cggtttgaaa atatgcctgc aatctgagcc agtgctttaa tggcatgtca     1020

gacagaactt gaatgtgtca ggtgaccctg atgaaaacat agcatctcag gagatttcat     1080

gcctggtgct tccaaatatt gttgacaact gtgactgtac ccaaatggaa agtaactcat     1140

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<211>   1182
<212>   DNA
<213>   Homo sapiens

<400>   446
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tggtgctgag ctccccactg gctttggctg gggacacccg accacgtttc ttgtggcagc      180

ttaagtttga atgtcatttc ttcaatggga cggagcgggt gcggttgctg gaaagatgca      240

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cggagctggg gcggcctgat gccgagtact ggaacagcca gaaggacctc ctggagcaga      360

ggcgggccgc ggtggacacc tactgcagac acaactacgg ggttggtgag agcttcacag      420

tgcagcggcg agttgagcct aaggtgactg tgtatccttc aaagacccag cccctgcagc      480

accacaacct cctggtctgc tctgtgagtg gtttctatcc aggcagcatt gaagtcaggt      540

ggttccggaa cggccaggaa gagaaggctg gggtggtgtc cacaggcctg atccagaatg      600

gagattggac cttccagacc ctggtgatgc tggaaacagt tcctcggagt ggagaggttt      660

acacctgcca agtggagcac ccaagtgtga cgagccctct cacagtggaa tggagagcac      720

ggtctgaatc tgcacagagc aagatgctga gtggagtcgg gggcttcgtg ctgggcctgc      780

tcttccttgg ggccgggctg ttcatctact tcaggaatca gaaaggacac tctggacttc      840

agccaacagg attcctgagc tgaaatgcag atgaccacat tcaaggaaga accttctgtc      900

ccagctttgc agaatgaaaa gctttcctgc ttggcagtta ttcttccaca agagagggct      960

ttctcaggac ctggttgcta ctggttcggc aactgcagaa aatgtcctcc cttgtggctt     1020

cctcagctcc tgcccttggc ctgaagtccc agcattgatg acagcgcctc atcttcaact     1080

tttgtgctcc cctttgccta aaccgtatgg cctcccgtgc atctgtactc accctgtacg     1140

acaaacacat tacattatta aatgtttctc aaagatggag tt                       1182
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<210>   447
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190

<210> 1410
<212> DNA
<213> Homo sapiens

<400> 447

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agaccccctgc atacataaag gtgcaaacca caagatggt gatgctgtcc tgcgaggcta     180

aaatctccct cagtaacatg cgcatctact ggctgagaca gcgccaggca ccgagcagtg     240

acagtcacca cgagttcctg gccctctggg attccgcaaa agggactatc cacggtgaag     300

aggtggaaca ggagaagata gctgtgtttc gggatgcaag ccggttcatt ctcaatctca     360

caagcgtgaa gccggaagac agtggcatct acttctgcat gatcgtcggg agccccgagc     420

tgaccttcgg gaagggaact cagctgagtg tggttgattt ccttcccacc actgcccagc     480

ccaccaagaa gtccaccctc aagaagagag tgtgccggtt acccaggcca gagacccaga     540

agggcccact ttgtagcccc atcacccttg gcctgctggt ggctggcgtc ctggttctgc     600

tggtttccct gggagtggcc atccacctgt gctgccggcg gaggagagcc cggcttcgtt     660

tcatgaaaca attttacaaa tgagcagaga atacggtttt ggtgtcctgc tacaaaaaga     720

catcggtcag taacgagcac gatgtggaaa aatgagagaa gggacacatt caaccctgga     780

gagttcaatg gctgctgaag ctgcctgctt ttcactgctg caaggccttt ctgtgtgtga     840

tgtgcatggg agcaacttgt tcgtgggtca tcgggaatac tagggagaag gtttcattgc     900

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cacttcatct tctcagctcc catttctact cttaagtttc tcagctccca tttctactct    1320

cccatggctt aatgcttctt tcattttctg tttgtttat acaaatgtct tagttgtaca    1380

aataaagtcc caggttaaag ataaaaaaaa                                      1410
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<210> 448
<211> 3084
<212> DNA
<213> Homo sapiens

<400> 448

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gggcaagaaa gacgcaagcc cagaggccct gccatttctg tgggctcagg tccctactgg    120

ctcaggcccc tgcctccctc ggcaaggcca caatgaaccg gggagtccct tttaggcact    180

tgcttctggt gctgcaactg gcgctcctcc cagcagccac tcagggaaag aaagtggtgc    240

tgggcaaaaa aggggataca gtggaactga cctgtacagc ttcccagaag aagagcatac    300

aattccactg gaaaaactcc aaccagataa agattctggg aaatcagggc tccttcttaa    360

ctaaaggtcc atccaagctg aatgatcgcg ctgactcaag aagaagcctt tgggaccaag    420

gaaactttcc cctgatcatc aagaatctta agatagaaga ctcagatact tacatctgtg    480

aagtggagga ccagaaggag gaggtgcaat tgctagtgtt cggattgact gccaactctg    540

acacccacct gcttcagggg cagagcctga ccctgacctt ggagagcccc cctggtagta    600

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ccgtgtctca gctggagctc caggatagtg gcacctggac atgcactgtc ttgcagaacc    720

agaagaaggt ggagttcaaa atagacatcg tggtgctagc tttccagaag gcctccagca    780

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cttggatcac ctttgacctg aagaacaagg aagtgtctgt aaaacgggtt acccaggacc    960

ctaagctcca gatgggcaag aagctcccgc tccacctcac cctgccccag gccttgcctc   1020

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aggaagtgaa cctggtggtg atgagagcca ctcagctcca gaaaaatttg acctgtgagg   1140

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ccggcttcac tggttgagtg ttgctctcta gtttccagag gcttaatcac accgtcctcc   1740

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cccactgctc atttggatcc caggggagtg ttcagggcca gccctggctg gcatggaggg   1860
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192

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cagatccaga ggtttctggc agccagtacc tcctgcccca tgctgcccgc ttctcaccct    2040

atgtgggtgg ggccacagac tcacatcctg accttgcaca aacagcccct ctggacacag    2100

ccccatgtac acggcctcaa gggatgtctc acatcctctg tctatttgag acttagaaaa    2160

atcctacaag gctggcagtg acagaactaa gatgatcatc tccagtttat agaccagaac    2220

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agaagcacag cacccatggg aagggtccat ctcagagaat ttacgagcag ggatgaaggc    2460

ctccctgtct aaaatccctc cttcatcccc cgctggtggc agaatctgtt accagaggac    2520

aaagcctttg gctcttctaa tcagagtgca agctgggagc acaggcactg caggagagaa    2580

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tctgcgcctg ccccacaccc tcccttaccc tcctccagac cattcaggac acagggaaat    2760

cagggttaca aatcttcttg atccacttct ctcaggatcc cctctcttcc tacccttcct    2820

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tttgtgccca ctctccaccc ctgctcccct gagctgaaat aaaaatacaa taaacttact    3000

ataaagataa aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa    3060

aaaaaaaaaa aaaaaaaaaa aaaa                                          3084


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<211>    1670
<212>    DNA
<213>    Homo sapiens

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ccctcctgga gaacttcagc tcttcctatg actatggaga aaacgagagt gactcgtgct     180

gtacctcccc gccctgccca caggacttca gcctgaactt cgaccgggcc ttcctgccag     240

ccctctacag cctcctcttt ctgctggggc tgctgggcaa cggcgcggtg gcagccgtgc     300

tgctgagccg gcggacagcc ctgagcagca ccgacacctt cctgctccac ctagctgtag     360
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cagacacgct gctggtgctg acactgccgc tctgggcagt ggacgctgcc gtccagtggg      420

tctttggctc tggcctctgc aaagtggcag gtgccctctt caacatcaac ttctacgcag      480

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accaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaa                  1670
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<211>   322
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<213>   Homo sapiens

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gctgagtgat ctggggggaca ctcaagcggt ttgtttctgt agaaatggga atcttaaggc      240

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ttaggtgggt ttgctttgcg ag   322


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<210>   451
<211>   568
<212>   DNA
<213>   Homo sapiens

<400>   451
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agccaaaggg caaaaaaaaa attttttta atcagggatg aggagggaag ctaagaattt     180

taaaatagta aatgaaaaat ttagaaatat gtattttgta gaaaatagta gacttagcac     240

taagatgaaa tgttttttggt aaagttttta atttgggagt tttgctgatt ccttcttacc     300

cttcaggaca attcacagat atcaatcctt tctggagtta cccctgactc cctcaacacc     360

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caggcgtggt ggctcatgcc tgtaatccta gcactttggg aggccaaggc aggagtcact     480

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gtctcgaact cttgatctca agtgatct                                      568


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<212>   DNA
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<400>   452
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taaaataatt aagggtatga ttaactctac ctgcacactg tcctattata ttcattcttt     660

ttgaaatgtc aaccccaagt tagttcaatc tggattcata tttaatttga aggtagaatg     720

ttttcaaatg ttctccagtc attatgttaa tatttctgag gagcctgcaa catgccagcc     780
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actgtgatag aggctggcgg atccaagcaa atggccaatg agatcattgt gaaggcaggg          840

gaatgtatgt gcacatctgt tttgtaactg tttagatgaa tgtcagttgt tatttattga          900

aatgatttca cagtgtgtgg tcaacatttc tcatgttgaa actttaagaa ctaaaatgtt          960

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agttttacag tgtttctggc ttagaacaaa ggggcttaat tattgatgtt ttcatagaga        1080

atataaaaat aaagcactta tag                                                  1103
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<210>   453
<211>   4156
<212>   DNA
<213>   Homo sapiens

<400>   453
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tggaggtgct ggggccttac gagcctctgc tgagtcgggt gcaggcagcc ctggtgtggg          240

agcggccagc taggagcgct ctgtggtgcc tggggctgaa cgcggctttc tggtgagaga          300

actggaccct cggaaaccct ccgagtcccg aattcgttgg ttcctctagg gctctacttc          360

tcgcctgccc tgttttcttc gctgcactgg ctccttcctg tacttgccta attttgcctc          420

acctccttcc actccatccc gcctgcaggc ttcggcaccc tagttcttcc cagggccgtc          480

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tctggtaaca tcttgagccg ctcaagagtg agcgagggct cctctttga gcccgacaaa          600

gctgcgtccc tttaaagcca tcacttcctt tctcttgtct gctcaagtgc aagttctaga          660

ttgtttccag aggttttagt agtttattgt tggagtagag gcgtgaagtc ttgcaaaggt          720

tttttgccct gacatctctt cgtcttgtgt ttttacttgc atttggcttg atgatcattg          780

tgtgtattga tcaatggaag aacaaaatct ggcctgaaat aaaagctggg gctttgtgca          840

ccctcggttg ctcagcgtgc ccgagctctg ccaccatgta gctgaagtct gggttagtgg          900

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197

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agggaaggaa ggagagcaaa atcttcggaa ggtgtttctt gtacctgagg gatcctgccc    4080

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<213>   Homo sapiens

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gatgctggtg gacttggcca agtccagggg cgtggaggcc gcccgggagc ggatgttcaa      360

tggtgagaag atcaactaca ccgagggtcg agccgtgctg cacgtggctc tgcggaaccg      420

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```
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cattgatgga actcacattg ccaaaaccct ggcccagctg aaccccgagt cctccctgtt    720

catcattgcc tccaagacct ttactaccca ggagaccatc acgaatgcag agacggcgaa    780

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ctgggattgg gtgggaggac gctactcgct gtggtcggcc atcggactct ccattgccct    960

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aattggctga agtgtttttg tgcagctgac ttttctgacc catgttcacg ttgttcacat   2040

cccatgtaga aaaataaaga tgccacggag gaggt                                2075
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<210> 455
<211> 1285
<212> DNA
<213> Homo sapiens

<400> 455

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aaaatctgta gaattcacgt tttgtaatga cactgtcgtc attccatgct ttgttactaa     240

tatggaggca caaaacacta ctgaagtata cgtaaagtgg aaatttaaag gaagagatat     300

ttacaccttt gatggagctc taaacaagtc cactgtcccc actgactta gtagtgcaaa      360

aattgaagtc tcacaattac taaaaggaga tgcctctttg aagatggata gagtgatgc     420

tgtctcacac acaggaaact acacttgtga agtaacagaa ttaaccagag aaggtgaaac    480

gatcatcgag ctaaaatatc gtgttgtttc atggttttct ccaaatgaaa atattcttat    540

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gaatgctact ggccttggtt taattgtgac ttctacaggg atattaatat tacttcacta    780

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aatgcatggc cctcttctga tttcaggttt gagtatctta gctctagcac aattacttgg    960

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gaagtgaagt gatggactcc gatttggaga gtagtaagac gtgaaggaa tacacttctg    1140

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<210> 456
<211> 1188
<212> DNA
<213> Homo sapiens

<400> 456

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gccgcgattc cgaggatgga gccgcgggag ccgtgggtgg agcaagaggg ccgcagtat     240

tgggagtgga ccacagggta cgccaaggcc aacgcacaga ctgaccgagt ggccctgagg     300
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accctgaggt gctgggccct gggcttctac cctgcggaga tcacgctgac ctggcagcgg    720

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cccaccatcc ccatcgtggg catcgttgct ggccttgttg tccttggagc tgtggtcact    960

ggagctgtgg tcgctgctgt gatgtggagg aagaagagct cagatagaaa cagagggagc    1020

tactctcagg ctgcagtcac tgacagtgcc cagggctctg gggtgtctct cacagctaat    1080

aaagtgtgag acagcttcct tgtgtgggac tgagaagcaa gatatcaatg tagcagaatt    1140

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<211>  1727
<212>  DNA
<213>  Homo sapiens

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atatatataa gaaacaagag ttctatttta gcacaaaggc attttatatt atttattgaa    480

tccataagtt tgttttcgtc aaaaacattc catattattt ctgctccttt ttatttgtat    540

agtttgttat ttaaagaaat ggcagtcctt cctgttctta atacaataaa attgaaataa    600

tgcacctagt aatgtggccg acatctcttc tcaccaccat ggactgtttt caacaacagt    660

tgatcttctg gtctgtgctg agaggcgcat gcatgtcttt cgtcacgtcg ggcagcacac    720
```

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gcacaccacc gtcagcacca ccgtttttac agttactttg gagctgctag actggttttc     1680

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<210> 458
<211> 1046
<212> DNA
<213> Homo sapiens

<400> 458
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ttattaagat acattggcaa gaaaagaaga gcaacacgat tctgggatcc caggagggga      180

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cactggacaa agaacacaga tgtatcgtca gacatgagaa taataaaaac ggaattgatc      300

aagaaattat ctttcctcca ataaagacag atgtcaccac agtggatccc aaagacagtt      360

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caaatgatgt catcacaatg gatcccaaag acaattggtc aaaagatgca aatgatacac      480

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atggagagaa atcataacag acggtggcac aaggaggcca tcttttcctc atcggttatt      660

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acagagaacc tcagtctgta ataacaatga ggaatagcca tggcgatctc cagcaccaat      840

ctctccatgt tttccacagc tcctccagcc aacccaaata gcgcctgcta tagtgtagac      900

agcctgcggc ttctagcctt gtccctctct tagtgttctt taatcagata actgcctgga      960

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<210> 459
<211> 169
<212> DNA
<213> Homo sapiens

<400> 459
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aaaaaaatat tgatttccag ctgaagtata gtacatctct gatgttttc                   169
```

<210> 460
<211> 4465
<212> DNA
<213> Homo sapiens

<400> 460
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atacagcaaa tccttgctgt tcccaccat gtcaaaaccg aggtgtatgt atgagtgtgg       240

gatttgacca gtataagtgc gattgtaccc ggacaggatt ctatggagaa aactgctcaa       300

caccggaatt tttgacaaga ataaaattat ttctgaaacc cactccaaac acagtgcact       360

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tcaagacaga tcataagcga gggccagctt tcaccaacgg gctgggccat ggggtggact       780
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203

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206

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208

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211

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ggtggaggct gacatcccag gccatgggca ggaagtcctc atcaggctct ttaagggtca    180

cccagagact ctggagaagt ttgacaagtt caagcacctg aagtcagagg acgagatgaa    240

ggcatctgag gacttaaaga agcatggtgc cactgtgctc accgccctgg gtggcatcct    300

taagaagaag gggcatcatg aggcagagat taagcccctg gcacagtcgc atgccaccaa    360

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gagcaagcat cccgggggact ttggtgctga tgcccagggg gccatgaaca aggccctgga    480

gctgttccgg aaggacatgg cctccaacta caaggagctg ggcttccagg gctaggcccc    540

tgccgctccc accccacccc atctgggccc cgggttcaag agagagcggg gtctgatctc    600

gtgtagccat atagagtttg cttctgagtg tctgctttgt ttagtagagg tgggcaggag    660

gagctgaggg gctggggctg gggtgttgaa gttggctttg catgcccagc gatgcgcctc    720

cctgtgggat gtcatcaccc tgggaaccgg gagtgccctt ggctcactgt gttctgcatg    780

gtttggatct gaattaattg tcctttcttc taaatcccaa ccgaacttct tccaacctcc    840

aaactggctg taaccccaaa tccaagccat taactacacc tgacagtagc aattgtctga    900

ttaatcactg gccccttgaa gacagcagaa tgtccctttg caatgaggag gagatctggg    960

ctgggcgggc cagctgggga agcatttgac tatctggaac ttgtgtgtgc ctcctcaggt   1020

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<210> 467
<211> 3144
<212> DNA
<213> Homo sapiens

<400> 467

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aagaggaaag tcactttact gaggggagtc tccattatca ttggcaccat cattggagca     180

ggaatcttca tctctcctaa gggcgtgctc cagaacacgg gcagcgtggg catgtctctg     240

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ggaacaacta aaagaaatc tggaggtcat tacacatata ttttggaagt ctttggtcca     360

ttaccagctt ttgtacgagt ctgggtggaa ctcctcataa tacgccctgc agctactgct     420

gtgatatccc tggcatttgg acgctacatt ctggaaccat tttttattca atgtgaaatc     480

cctgaacttg cgatcaagct cattacagct gtgggcataa ctgtagtgat ggtcctaaat     540

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gcaattctga taattatagt ccctggagtt atgcagctaa ttaaaggtca aacgcagaac     660

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tatggaatgt atgcatatgc tggctggttt tacctcaact ttgttactga agaagtagaa     780

aaccctgaaa aaaccattcc ccttgcaata tgtatatcca tggccattgt caccattggc     840

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cgcaagcaca ctcctctacc agctgttatt gttttgcacc ctttgacaat gataatgctc    1140

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tcagagaaaa taaccagaac attacaaata atactggaag ttgtaccaga agaagataag    1500

ttatgaacta atggacttga gatcttggca atctgcccaa ggggagacac aaaatanggga    1560

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213

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cagttatttt tattcatata ttttagcata ttcgaactaa tttctaagaa atttagttat      1680

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gtctctgata cctacctatt ggggttagga gaaaagacta gacaattact atgtggtcat      1800

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tatatatggg ttttgtaaag atggttttac acactacaga tgtctatact gtgaaaagtg      1920

ttttcaattc tgaaaaaaag catacatcat gattatggca aagaggagag aaagaaattt      1980

attttacatt gacattgcat tgcttcccct tagataccaa tttagataac aaacactcat      2040

gctttaatgg attataccca gagcactttg aacaaaggtc agtggggatt gttgaataca      2100

ttaaagaaga gtttctaggg gctactgttt atgagacaca tccaggagtt atgtttaagt      2160

aaaaatcctt gagaatttat tatgtcagat gtttttttcat tcattatcag gaagtttttag      2220

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agcaagagtt agtttggtat taaatcctca ttagaacaac cacctgtttc actaataact      2340

tacccctgat gagtctatct aaacatatgc attttaagcc ttcaaattac attatcaaca      2400

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ctacatgcaa tgttagtaat tctgaagttt tttaaattta tggctatttt tacacgatga      2520

tgaattttga cagtttgtgc attttctta tacatttat attcttctgt taaaatatct      2580

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caacatggag aaacccatc tctactaaaa atacaaaatt agctgggcat ggtggcacat      3000

gctggtaatc tcagctattg aggaggctga ggcaggagaa ttgcttgaac ccgggaggcg      3060

gaggttgcag tgagccaaga ttgcaccact gtactccagc ctgggtgaca aagtcagact      3120

ccatctccaa aaaaaaaaa aaaa                                             3144
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<210> 468
<211> 1177
<212> DNA
<213> Homo sapiens

<400> 468
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tgaccgctgt ccatccagaa ccacccactg catgcagaga aaaacagtac ctaataaaca    180

gtcagtgctg ttctttgtgc cagccaggac agaaactggt gagtgactgc acagagttca    240

ctgaaacgga atgccttcct tgcggtgaaa gcgaattcct agacacctgg aacagagaga    300

cacactgcca ccagcacaaa tactgcgacc ccaacctagg gcttcgggtc cagcagaagg    360

gcacctcaga aacagacacc atctgcacct gtgaagaagg ctggcactgt acgagtgagg    420

cctgtgagag ctgtgtcctg caccgctcat gctcgcccgg ctttggggtc aagcagattg    480

ctacaggggt ttctgatacc atctgcgagc cctgcccagt cggcttcttc tccaatgtgt    540

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tggtggtgat ccccatcatc ttcgggatcc tgtttgccat cctcttggtg ctggtctttta   720

tcaaaaaggt ggccaagaag ccaaccaata aggcccccca ccccaagcag gaaccccagg    780

agatcaattt tcccgacgat cttcctggct ccaacactgc tgctccagtg caggagactt    840

tacatggatg ccaaccggtc acccaggagg atggcaaaga gagtcgcatc tcagtgcagg    900

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cagagagcct ggtgctgctg ctgctgtggc gtgagggtga ggggctggca ctgactgggc   1020

atagctcccc gcttctgcct gcacccctgc agtttgagac aggagacctg gcactggatg   1080

cagaaacagt tcaccttgaa gaacctctca cttcaccctg gagcccatcc agtctcccaa   1140

cttgtattaa agacagaggc agaaaaaaaa aaaaaaa                             1177
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cgcccagctt ggaggtgcta actccagagg ccagcatcag caactgggca cagaaaggag    180

ccgcctgggc agggaccatg gcacggccac atccctggtg gctgtgcgtt ctggggaccc    240

tggtggggct ctcagctact ccagccccca gagctgccc agagaggcac tactgggctc     300

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agcatagaaa ggctgctcag tgtgatcctt gcataccggg ggtctccttc tctcctgacc    420

accacacccg gccccactgt gagagctgtc ggcactgtaa ctctggtctt ctcgttcgca    480
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actgcaccat cactgccaat gctgagtgtg cctgtcgcaa tggctggcag tgcagggaca    540

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ctacccactg gccaccccaa agatccctgt gcagctccga ttttattcgc atccttgtga    780

tcttctctgg aatgttcctt gttttcaccc tggccggggc cctgttcctc catcaacgaa    840

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aaa                                                                   1323
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<212> DNA
<213> Homo sapiens

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atccccagtg cactatggga ctgagtaaca ttctctttgt gatggccttc ctgctctctg    180

gtgctgctcc tctgaagatt caagcttatt caatgagac tgcagacctg ccatgccaat     240

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tcaaggacaa gggcttgtat caatgtatca tccatcacaa aaagcccaca ggaatgattc    480

gcatccacca gatgaattct gaactgtcag tgcttgctaa cttcagtcaa cctgaaatag    540

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ttttctgtct aattctatgg aaatggaaga agaagaagcg gcctcgcaac tcttataaat    960

gtggaaccaa cacaatggag agggaagaga gtgaacagac caagaaaaga gaaaaaatcc   1020

atatacctga aagatctgat gaagcccagc gtgtttttaa aagttcgaag acatcttcat   1080

gcgacaaaag tgatacatgt ttttaattaa agagtaaagc ccatacaagt attcattttt   1140

tctacccttt cctttgtaag ttcctgggca accttttga tttcttccag aaggcaaaaa   1200

gacattacca tgagtaataa gggggctcca ggactccctc taagtggaat agcctccctg   1260

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tggaagcaga gctggggagg gagagccatc accttgataa tgggatgaat ggaaggaggc   2220

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ccacaaaaat gttcctttat tttatgtaaa ccctcaaggg ttatagactg ccatgctaga   2580
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217

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caagcttgtc catgtaatat tcccatgttt ttaccctgcc cctgccttga ttagactcct    2640

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aaaaaaaaaa aaaaaaaaaa a                                             2781
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<213>   Homo sapiens

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gcttcaaagg tgagggggaa actgtaggcg gtggagacag ggctgggggt aggagggtta    180

ggatttccac aagaacaagg caggaacagc agagataaaa agtttacttt tgtggtagca    240

aaaggggaac ctgcctttat tgccctcctg ccacactgcg gtccctttcc cgggcctgcc    300

tctctcagca tccctctag ctccttacac cctagcgggg cccctcaact ccccaacccc    360

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acaggccccc cagccaagaa agctatctct gagttgccct gatttgaagg gaaaagggat    1260

gatgggattg aaggggcttc taatgaccca gatatggaaa cagaagacaa aattgtaagc    1320

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<210> 472
<211> 1080
<212> DNA
<213> Homo sapiens

<400> 472
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aaagctgttc acaaaggcaa gcctccctga ccgttcccag taggtgttga tgcacaggga     180

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<211> 195
<212> DNA
<213> Homo sapiens

<400> 473
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tccgagggga ccctctggcc cgataccggg gggcccgggc cgggttggtc cagggccttc     180

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<210> 474

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<211>  249
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<213>  Homo sapiens

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gttgactagt tcatgagatt ctgctgtacg tgtgatggtt attcgctggt tcgttctaag   180

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cgagttctgc caggacatct ttctcggggt tctcgttgca atcctcggtc actngttcaa     60

angttttgag ggattcttcg gccaactctg gaaacagcgg gtctcccagn ctcagctgac   120
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tgttaacctc cttcctnaac atagtctgca ggaacgtcgt ggccttggtc acgggtgtct   180

cgggc   185

<210> 477
<211> 300
<212> DNA
<213> Homo sapiens

<220>
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<223> n is a, c, g, t or u

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<222> (17)..(17)
<223> n is a, c, g, t or u

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<221> misc_feature
<222> (32)..(32)
<223> n is a, c, g, t or u

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<221> misc_feature
<222> (34)..(35)
<223> n is a, c, g, t or u

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<222> (50)..(50)
<223> n is a, c, g, t or u

<220>
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<222> (103)..(103)
<223> n is a, c, g, t or u

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<222> (110)..(110)
<223> n is a, c, g, t or u

<220>
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<222> (116)..(116)
<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<222> (134)..(135)
<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<223> n is a, c, g, t or u

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<222> (172)..(172)
<223> n is a, c, g, t or u

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<222> (182)..(182)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (197)..(197)
<223> n is a, c, g, t or u

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<221> misc_feature
<222> (204)..(204)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (257)..(257)
<223> n is a, c, g, t or u

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tggtggtctt agggaaggct gagttcttgg taaagaactc tanattcctn tagcanatat   120

anatcatctt tctnntaagt tcatccttnt tngcacggnc cttagcctnc antgcacccc   180

cnaacttgtt agcggcnccc ttgntcacat catgcagctc cttaatacaa gccatccaca   240

tctcccgctt atcctcnggt acaatgtagt tctcatacat gctctgcata gttagcccaa   300

<210> 478
<211> 363
<212> DNA

<213> Homo sapiens

<400> 478
cttgacagcc cggcaggcag catccctgat attccttgcg gtatatggtg tgatgtcgtg   60

tggaggcaac catggcggca cattgtcttc cgtgtctaaa agatggccgg acaaggcagc   120

ccgtcttctc cgccttcgcc tgatgcgctg catccagcct ctgttttcat cacccctgct   180

ttgcccccaa ggttgctgat ctcttgagta tgactcttct ggtaccaatc tctcagaagc   240

cccactggat ggaggccccg gcccagggtc ctgatcatgc tcgccggtag tctgtacatt   300

atctccccgc tcattgtcgg gtgactgtct agagtccccc tgtccttcaa atgattccat   360

ggt   363

<210> 479
<211> 600
<212> DNA
<213> Homo sapiens

<400> 479
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aacatccagg cttgggcaca tctgcttcaa caggaggcgc agcctgtcat tttcagatga   120

tttggcagca gccacctcac ggtagtgctg cagcagttgc ttaaacttgg cccggcattt   180

tctggaagcc acccgattct tgtatcgctt tatttctagt tcagaatcgc attcctccag   240

cgattctggc tgttgtggtt tccgtgtgcg tcgtgccggg gcagccactg gtgcaggctg   300

tggaacacca atgtctgcta gctgttgtcc ttggttagcc ccggggcaag caaacaccac   360

tgctgctgct gtttgaacag tagaattgtc tccaggttga ggtgcttctc ccccggcttg   420

gttagtctgt tgattctggg ttatgtcgga gactgggaac agctgaggtg ctgcataagc   480

ttgataagca ttctcaggag caggctgagg ggcagaaaac cacgacccag tcggagcggt   540

tgaaacatga taggcagtta gctggccttg tggcagaggc tctggcagca ccggccacag   600

<210> 480
<211> 146
<212> DNA
<213> Homo sapiens

<400> 480
ccctgaaggt gaaccgctta ccacctcctc ttcttgctgg acgaggaccc ttctacggac   60

tcgtctgggt tcttggcccc ctctggtagg actgggcgac cggtgccttc ttaggagctg   120

tccgagggga ccctctggcc cgatac   146

<210> 481
<211> 66
<212> DNA

<213> Homo sapiens

<400> 481
cctaggggag accgaagtga aggccctgga ccaacccggc ccgggccccc cggtatcggg   60

ccagag   66

<210> 482
<211> 176
<212> DNA
<213> Homo sapiens

<400> 482
cctctacagt caaacagatt aaggttcgag tggacatgct gcggcataga atcaaggagc   60

acatgctgaa aaaatatacc cagacggaag agaaattcac tggcgccttt aatatgatgg   120

gaggatgttt gcagaatgcc ttagatatct tagataaggt tcatgagcct ttcgag   176

<210> 483
<211> 185
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (54)..(54)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (62)..(62)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (110)..(110)
<223> n is a, c, g, t or u

<220>
<221> misc_feature
<222> (137)..(137)
<223> n is a, c, g, t or u

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angttttgag ggattcttcg gccaactctg gaaacagcgg gtctcccagn ctcagctgac   120

tgttaacctc cttcctnaac atagtctgca ggaacgtcgt ggccttggtc acgggtgtct   180

cgggc   185

<210> 484
<211> 641
<212> DNA
<213> Homo sapiens

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ccagaaggag acaacaatgt ccctgctacc cgtgccatac acagaggctg cctctttgtc     120

tactggttct actgtgacaa tcaaagggcg accacttgcc tgtttcttga atgaaccata     180

tctgcaggtg gatttccaca ctgagatgaa ggaggaatca gacattgtct tccatttcca     240

agtgtgcttt ggtcgtcgtg tggtcatgaa cagccgtgag tatggggcct ggaagcagca     300

ggtggaatcc aagaatatgc cctttcagga tggccaagaa tttgaactga gcatctcagt     360

gctgccagat aagtaccagg taatggtcaa tggccaatcc tcttacacct ttgaccatag     420

aatcaagcct gaggctgtga agatggtgca agtgtggaga gatatctccc tgaccaaatt     480

taatgtcagc tatttaaaga gataaccaga cttcatgttg ccaaggaatc cctgtctcta     540

cgtgaacttg ggattccaaa gccagctaac agcatgatct tttctcactt caatccttac     600

tcctgctcat taaaacttaa tcaaacttca aaaaaaaaaa a                          641


<210>  485
<211>  2165
<212>  DNA
<213>  Homo sapiens

<400>  485
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tagtgctcgg cgtcagacat ggcggaggcg atggatttgg gcaaagaccc caacgggccc     180

acccattcct cgactctgtt cgtgagggac gacggcagct ccatgtcctt ctacgtgcgg     240

cccagcccgg ccaagcgtcg gctgtcgacg ctcatcctgc acggcggcgg caccgtgtgc     300

cgagtgcagg agcccggggc cgtgctgctg gcccagcccg gggaggcgct ggccgaggcc     360

tcgggtgatt tcatctccac gcagcacatc ctggactgcg tggagcgcaa cgagaggctg     420

gagctggagg cctatcggct gggccccgcc tcggcggcgg acaccggctc ggaagcaaag     480

cccgggggcc tggccgaggg cgccgcggag ccggagccgc agcggcacgc cgggcggatc     540

gccttcacgg atgcggacga cgtagccatc cttacctacg tgaaggaaaa tgcccgctcg     600

cccagctccg tcacaggtaa cgccttgtgg aaagcgatgg agaagagctc gctcacgcag     660

cactcgtggc agtccctgaa ggaccgctac ctcaagcacc tgcggggcca ggagcataag     720

tacctgctgg gggacgcgcc ggtgagcccc tcctcccaga gctcaagcg gaaggcggag     780

gaggacccgg aggccgcgga tagcggggaa ccacagaata agagaactcc agatttgcct     840

gaagaagagt atgtgaagga agaaatccag gagaatgaag aagcagtcaa aaagatgctt     900
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225

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gtggaagcca cccgggagtt tgaggaggtt gtggtggatg agagccctcc tgattttgaa     960

atacatataa ctatgtgtga tgatgatcca cccacacctg aggaagactc agaaacacag    1020

cctgatgagg agtaagaaga agaagaagaa aaagtttctc aaccagaggt gggagctgcc    1080

attaagatca ttcggcagtt aatggagaag tttaacttgg atctatcaac agttacacag    1140

gccttcctaa aaaatagtgg tgagctggag gctacttccg ccttcttagc gtctggtcag    1200

agagctgatg gatatcccat ttggtcccga caagatgaca tagatttgca aaaagatgat    1260

gaggatacca gagaggcatt ggtcaaaaaa tttggtgctc agaatgtagc tcggaggatt    1320

gaatttcgaa agaaataatt ggcaagataa tgagaaaaga aaaaagtcat ggtaggtgag    1380

gtggttaaaa aaaattgtga ccaatgaact ttagagagtt cttgcattgg aactggcact    1440

tattttctga ccatcgctgc tgttgctctg taagtcctag atttttgtag ccaagcagag    1500

ttgtagaggg ggataaaaag aaaagaaatt ggatgtattt acagctgtcc ttgaacaagt    1560

atcaatgtgt ttatgaaagg aagatctaaa tcagacagga gttggtctac atagtagtga    1620

tccattgttg gaatggaacc cttgctatag tagtgacaaa gtgaaaggaa atttaggagg    1680

cataggccat ttcaggcagc ataagtaatc tcctgtcctt ggcagaagc tcctttagat     1740

tgggatagat tccaaataaa gaatctagaa ataggagaag atttaattat gaggccttga    1800

acacggatta tccccaaacc cttgtcattt cccccagtga gctctgattt ctagactgct    1860

ttgaaaatgc tgtattcatt ttgctaactt agtatttggg taccctgctc tttggctgtt    1920

cttttttggg agcccttctc agtcaagtct gccggatgtc tttctttacc taccctcag     1980

ttttccttaa aacgcgcaca caactctaga gagtgttaag aataatgtta cttggttaat    2040

gtgttattta ttgagtattg tttgtgctaa gcattgtgtt agatttaaaa aattagtgga    2100

ttgactccac tttgttgtgt tgttttcatt gttgaaaata aatataactt tgtattcgaa    2160

aaaaa                                                               2165
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<210> 486
<211> 1098
<212> DNA
<213> Homo sapiens

<400> 486
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cagacctggg cgggctccca ctccatgagg tatttcttca catccgtgtc ccggcccggc     120

cgcggggagc cccgcttcat cgccgtgggc tacgtggacg acacgcagtt cgtgcggttc     180

gacagcgacg ccgcgagcca gaggatggag ccgcgggcgc cgtggataga gcaggagggg     240

ccggagtatt gggaccagga gacacggaat gtgaaggccc agtcacagac tgaccgagtg     300
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226

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gacctggggga ccctgcgcgg ctactacaac cagagcgagg ccggttctca caccatccag      360

ataatgtatg gctgcgacgt ggggtcggac gggcgcttcc tccgcgggta ccggcaggac      420

gcctacgacg gcaaggatta catcgccctg aacgaggacc tgcgctcttg daccgcggcg      480

gacatggcgg ctcagatcac caagcgcaag tgggaggcgg cccatgaggc ggagcagttg      540

agagcctacc tggatggcac gtgcgtggag tggctccgca gatacctgga gaacgggaag      600

gagacgctgc agcgcacgga cccccccaag acacatatga cccaccaccc catctctgac      660

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tacacctgcc atgtgcagca tgagggtctg cccaagcccc tcaccctgag atgggagctg      900

tcttcccagc ccaccatccc catcgtgggc atcattgctg gcctggttct ccttggagct      960

gtgatcactg gagctgtggt cgctgccgtg atgtggagga ggaagagctc agatagaaaa      1020

ggagggagtt acactcaggc tgcaagcagt gacagtgccc agggctctga tgtgtccctc      1080

acagcttgta aagtgtga                                                    1098
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<210>   487
<211>   242
<212>   DNA
<213>   Homo sapiens

<400>   487
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caacaagaag gttgaattgt tacccagtaa ctttcattct tcttagggta tgaaaattgg      120

ccactgaatg ttctgttcca aaattcccta agcaagttaa gctaaatatc tggattaaaa      180

gatttatttt gattttaaaa tggacactac atatctggct tatttagtct gccctcgtgc      240

cg                                                                     242
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<210>   488
<211>   3415
<212>   DNA
<213>   Homo sapiens

<400>   488
ccccctcccc tcctgcagcc tcctgcgccc cgccgagctg gcggatggag ctgcgcagcg       60

ggagcgtggg cagccaggcg gtggcgcgga ggatggatgg ggacagccga gatggcggcg      120

gcggcaagga cgccaccggg tcggaggact acgagaacct gccgactagc gcctccgtgt      180

ccacccacat gacagcagga gcgatggccg ggatcctgga gcactcggtc atgtacccgg      240

tggactcggt gaagacacga atgcagagtt tgagtccaga tcccaaagcc cagtacacaa      300
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gtatctacgg agccctcaag aaaatcatgc ggaccgaagg cttctggagg cccttgcgag      360

gcgtcaacgt catgatcatg ggtgcagggc cagcccatgc catgtatttt gcctgctatg      420

aaaacatgaa aaggacttta aatgacgttt tccaccacca aggaaacagc cacctagcca      480

acggtatttt gaaagcgttt gtctggagtt agaaagttct cttcttcaac acgtccctcc      540

ccagggtgtt cctccctgtg acccagccgc ctcgacttcg gcccgcttgc tcacgaataa      600

agaactcaga gttgtgtgtg caatgcacac ccagacacac gcacgcacac acgcgcgc        660

gcacacacat gctttttttc tgttcccctc cgctttctga agcctgggga gaaatcagtg      720

acagaggcgc tctctgggtt ttattgttat gtgggttttc ttttgtattt tttttgtttg      780

ttttgttttt aaacattcaa aagcaattaa tgatcagaca taggagaaac cctgaataga      840

aacaaaactt ttgaatgctg gattcaaaaa agaaaaaaag ttatctggac agcttctttg      900

agactattta aaaactggta caacaggtct ctacaacgcc aagatctaac taagctttaa      960

aaggtcaaga agttttatgg ctgacaaagg actcgcgcaa cgcagaaggc ctttcccacc     1020

ttaagcttcc ggggatctgg gaattttacc cccattctct tctgtttgtc tgagtctcat     1080

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gttcttgaag ccaggcctga cccgactctc agatggggtc agtcccgtcg ctttgcagac     1920

tgaccctgga aatctacaaa atgcagattt tcctgatttc ctcttctctt gcccagtttt     1980

tttttttttt tttttttttt tttttaaagc ctggattgta accagatttt cttttttccc     2040

ccttctcagc tgtagatatg atatctcctt tcagggcccc agcttaaggg caaagtgagt     2100
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taatgtgtag acaaaggcga gggacaagag agagttaaca tctagacagt ggaaaaagcc    2160

atggtgtgtg gtttctggga accaccaaca cttgcaggtt tagcttttc ccagggttga    2220

ctacaagaaa gaaaaccatg tttttgcaag attaaaatgt ggttgagtgt gcctaaatta    2280

accatcccca tttttatcat atttccacca tcacttcagg gttttaagag tcagtgctca    2340

cctgggcgga gctggtagta cattttgctt cttagaaagc taagtcctgg gttccgtctg    2400

attttaggtt ccaggaactt cctgagaaca cccgatcgca gagggtaatt ttctggagtt    2460

tgttttgcag ggatagctgg gagtatggcc accctgctcc acgatgcggt aatgaatcca    2520

gcagaagtgg tgaagcagcg cttgcagatg tacaactcgc agcaccggtc agcaatcagc    2580

tgcatccgga cggtgtggag gaccgagggg ttgggggcct tctaccggag ctacaccacg    2640

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gccgggggccc tcgccgcggc cgccacgacc ccctggacg tctgtaagac ccttctgaac    2820

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aagtactttc tcaccaagcg ccagctggaa aatcgagctc catactaaag gaagggatca    3060

tagaatcttt tcttaaagtc attctctgcc tgcatccagc cccttgccct ctcctcacac    3120

gtagatcatt ttttttttg cagggtgctg cctatgggcc ctctgctccc caatgcctta    3180

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gggcagaatg tagctttct gcttcactgt ggcagcctcc tccctggatc cttagatccc    3360

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<210> 489
<211> 2473
<212> DNA
<213> Homo sapiens

<400> 489
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tgcgccgccg ctcgggcgcc gggctccgtc gcggccgcag ccccgcgggt cgccctcccg     120

tgcctcgccc gcggacaccc tggccgtgga caccctggcc gtgggcaccc gcggggcgcg     180

gcgcgggcgc tgcgcggcgg cggcggcggc atgaaggtca cgtcgctcga cgggcgccag     240

ctgcgcaaga tgctccgcaa ggaggcggcg gcgcgctgcg tggtgctcga ctgccggccc     300
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tatctggcct tcgctgcctc gaacgtgcgc ggctcgctca acgtcaacct caactcggtg    360

gtgctgcggc gggcccgggg cggcgcggtg tcggcgcgct acgtgctgcc cgacgaggcg    420

gcgcgcgcgc ggctcctgca ggagggcggc ggcggcgtcg cggccgtggt ggtgctggac    480

cagggcagcc gccactggca gaagctgcga gaggagagcg ccgcgcgtgt cgtcctcacc    540

tcgctactcg cttgcctacc cgccggcccg cgggtctact tcctcaaagg gggatatgag    600

actttctact cggaatatcc tgagtgttgc gtggatgtaa aacccatttc acaagagaag    660

attgagagtg agagagccct catcagccag tgtggaaaac cagtggtaaa tgtcagctac    720

aggccagctt atgaccaggg tggcccagtt gaaatccttc ccttcctcta ccttggaagt    780

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gtctcccgac ggacctccga ggcctgcatg acccacctac actacaaatg gatccctgtg    900

gaagacagcc acacggctga cattagctcc cactttcaag aagcaataga cttcattgac    960

tgtgtcaggg aaaagggagg caaggtcctg gtccactgtg aggctgggat ctcccgttca   1020

cccaccatct gcatggctta ccttatgaag accaagcagt tccgcctgaa ggaggccttc   1080

gattacatca agcagaggag gagcatggtc tcgcccaact ttggcttcat gggccagctc   1140

ctgcagtacg aatctgagat cctgccctcc acgcccaacc cccagcctcc ctcctgccaa   1200

ggggaggcag caggctcttc actgataggc catttgcaga cactgagccc tgacatgcag   1260

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238

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242

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243

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245

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246

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<213> Homo sapiens

<400> 505

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248

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<212> DNA
<213> Homo sapiens

<400> 507

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cgccgggcgg gatgggccgg cgccgggcgc cagagctgta ccgggctccg ttcccgttgt   180

acgcgcttca ggtcgacccc agcactgggc tgctcatcgc tgcgggcgga ggaggcgccg   240

ccaagacagg cataaagaat ggcgtgcact ttctgcagct agagctgatt aatgggcgct   300

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tggctggtga catccttgct gcagggcagg atgcacactg tcagctcctg cgcttccagg   420

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aagatgcaat aagttcctag gtagtctacc cttaccttga ggaatgggaa aatgaacctc    1980

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<213>  Homo sapiens

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252

<211> 1406
<212> DNA
<213> Homo sapiens

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cctgggatgt tcaagttcat gaccagaaga taaagaagc tactgaaaaa gctagacatg      360

aaacctttgc tgctgaaatg aggcaaaatg acaaaatcat gtgcatattg gaaaaccgga     420

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cagcccggca gtcagataat gatgttcgga atacgatatc aggaatgcag aaattcatgg     600

gagaggattt aaacttccat gagaggaaga aattccaaga ggaacaaaac agagaatggt     660

ctttgcagca gcaaagggaa tggaagaacg cccgtgctga acaaaaatgc gcagaggccc     720

tctacacaga gacaaggctg cagtttgacg agacagccaa gcacctccag aagctggaaa     780

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<211> 4357
<212> DNA
<213> Homo sapiens

<400> 510

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<212> DNA
<213> Homo sapiens

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266

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<213>   Homo sapiens

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agaaactaaa tgatcgcatg gtacatgctt gtattatata gatgggttta ggaatctata      120

aagtatggag gtaggaagac accatatgtc caggatcaaa acattcctca tattgaggta      180

gtctagtgaa gctgtttcat gtagctgctt taggaagtgg tttaaggaag cttactccca      240

cttcaagtta agcaccaaag caatcactaa ttctggagca caggaagact gctatctcat      300
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cattcacctt tgcag   315

<210>   523
<211>   972
<212>   DNA
<213>   Homo sapiens

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atgacaccga cgacgacgac cgcggaactc acgacggagt ttgactacga tgaagacgcg   60

actccttgtg ttttcaccga cgtgcttaat cagtcaaagc cagttacgtt gtttctgtac   120

ggcgttgtct ttctcttcgg ttccatcggc aacttcttgg tgatcttcac catcacctgg   180

cgacgtcgga ttcaatgctc cggcgatgtt tactttatca acctcgcggc cgccgatttg   240

cttttcgttt gtacactacc tctgtggatg caatacctcc tagatcacaa ctccctagcc   300

agcgtgccgt gtacgttact cactgcctgt ttctacgtgg ctatgtttgc cagtttgtgt   360

tttatcacgg agattgcact cgatcgctac tacgctattg tttacatgag atatcggcct   420

gtaaaacagg cctgcctttt cagtattttt tggtggatct ttgccgtgat catcgccatt   480

ccacacttta tggtggtgac caaaaaagac aatcaatgta tgaccgacta cgactactta   540

gaggtcagtt acccgatcat cctcaacgta gaactcatgc ttggtgcttt cgtgatcccg   600

ctcagtgtta tcagctactg ctactaccgc atttccagaa tcgttgcggt gtctcagtcg   660

cgccacaaag gtcgcattgt acgggtactt atagcggtcg tgcttgtctt tatcatcttt   720

tggctgccgt accacctaac gctgtttgtg gacacgttaa aactcctcaa atggatctcc   780

agcagctgcg agttcgaaag atcgctcaaa cgtgcgctca tcttgaccga gtcgctcgcc   840

ttttgtcact gttgtctcaa tccgctgctg tacgtcttcg tgggcaccaa gtttcgcaag   900

aactacactg tctgctggcc gagtttcgcc agcgactctt ttcccgcgat gtatcctggt   960

accacagcat ga   972

<210>   524
<211>   949
<212>   DNA
<213>   Homo sapiens

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ctgcaattgc acgtttctgc cctttacaat aaagaaacac acactttcct ttcaccaccc   180

acacccacca aaaataccac cacactccaa cacaccccac gaagaaagcg agaaagccca   240

aaactgggcc ccccaccaca accgcacccc cacgaatctg tcatacatcc acaagacacc   300

cgggccctct gagcacccac ggcgaacggc cgccaagccg ccaccccct cccaggcggc   360

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agccccaca  tgcgccacgt  cgtacatcac  gtcacccaac  gccaccgacc  tatgcgcaat    420

cgcgcgcata  gccccgtact  cgggccagca  gccccacccc  agccagccac  actgctcccc    480

ctcgcacacc  acaccaagat  cgcgcgaccc  aacgcaccca  ctccgcacca  caccccacac    540

caccccacc   ccgctcgacc  agcatgtgtc  acaaccccgt  acccgcaccc  tgagtaccac    600

gaaacggaca  ggctaacgac  gcgaagtacc  tcacccaccc  gaccgaacgc  gatccacggt    660

cccgtaagcg  ctaattccag  actacacccc  catagctcgc  cgcaatggtc  tgcacgtcca    720

ccccacacca  acagagatca  ctacagaaat  atgcctccaa  ccccgcccac  gttaaactcc    780

ccactccaca  cgcagcaatg  tcactcggca  ccgcgccttt  cacggtgtga  caggtcttct    840

ccatagatgt  cggatcggcc  tccttactac  ctcccccctt  acgaaagagt  acacactcca    900

caaccacaga  cctccgccca  aggcgccgcc  cgcgcgcccc  gcgcacgtg                 949
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<210>  525
<211>  2298
<212>  DNA
<213>  Homo sapiens

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ggacacactt  actgcagttg  ttcaaaatgc  caaaaaaaat  ggaagatatg  atatgggaat   180

cttagatctt  ggttctggag  atgaaaaagt  gcggaaaagt  gatgttaaaa  agtttctgac   240

tccaggatat  tcaacctctg  gccacgtaga  attatacaca  attagtgtag  agaggggaat   300

gtcatgggag  gaagctacca  agatttgggc  tgagctgaca  ggaccagacg  atggctttta   360

cttgtcattg  caaataagga  acaacaagaa  aactgccatc  ttagttaaag  aagtgaatcc   420

taaaaagaaa  cttttcttag  tttatcgacc  aaatactggg  aagcagctca  aattagaaat   480

ttatgctgat  ctaaaaaaga  aatataagaa  ggtcgtctca  gatgatgccc  tgatgcactg   540

gttagatcag  tataattcat  ctgcagatac  ttgtactcat  gcttattggc  gcggcaattg   600

caaaaaagca  agcttggggc  tagtttgtga  ataggtctt   cgttgccgta  catattatgt   660

attatgtggt  tcagtgctga  gtgtctggac  aaaagttgag  ggtgttctag  catctgtcag   720

tggcacaaac  gtgaagatgc  agatcgtgcg  gctaagaacg  gaagatgggc  aacggattgt   780

aggtttgatc  attccggcaa  attgtgtgtc  tcctcttgta  aatctcctat  caacttcaga   840

ccagtctcaa  cagcttgcgg  tccaacagaa  acagctatgg  caacagcatc  accctcagag   900

catcaccaac  ttgagcaacg  catgaagaac  agacaggttt  caacatggat  ggatctgaaa   960

tgctgttgaa  gcatatcatt  tgcataaaaa  tcagggacag  tttccaaaga  attatatatt  1020
```

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tttttcagtt gtgctctcta gttagttttt ttgggagtaa ggacaaacct ggaatagata    1080

gcaaaactga aaatcagcag tgctgatggt ggtacatatg tctttccttt agcttctccc    1140

ctgataattc ccatctgctt ttacttcggg tgagcagagg gggatgtgtg tgtgcgtgtg    1200.

tgtcagtctg tttgtgagtg tgttaaaggc tacagaccac agttggttta aaatgcttgg    1260

aacttcccaa actggcttta ctttatgttt atacagtgct cagggttaac gcagtacatc    1320

catgccattg ctgtgggagg tatccccgga tgcatgtgtt ttgagtctat aaatatagaa    1380

aatatatatt ggtttctttt tccaacttaa taggtttatt aaagcatgaa atgaaaggtt    1440

gcatatcatg cattcaggtt attttctaat ttttgttctg acagtgcatg tctttggaag    1500

catgctgaaa caagattaac acaggagtcg agtaacagag agaaacattt gttagatgta    1560

cagcattggt tattgcattt ttatagtgtt tatacctggg tattgcttca aaccctgcag    1620

acccctcctt cccccttctcc ctgccctggg tttctggtca aggtaatgaa tacatacatt    1680

tttctgtgat aaaactctta aaagttaatt ttaatgtatt aatagtattc ctaatgtgtg    1740

ctgcagaaat ggctatgagc ctcttaaatt tacatttgca acttaaaggt agttttagaa    1800

ggaagtacaa attggctttc atcttgcaaa caatcgtttt ttacttcatt atcttaattt    1860

gctttgtcac tcataaaaag gaaaccatac ctgagttgta gacaatgagg aaacacttga    1920

ggcttctgct gtgtgttctt ttgttattgt tgttattgtt gttactcagt aacttgaata    1980

ttgtttaatg tgttgtaaga cgtagagttt atctcaagct gttaaaaatg gtaatgtaca    2040

aatgtgaata gacacttatc tatataatat gggtaagttt tgtttcgcct ataatagatg    2100

tttataaaaa caagtgaggg gacagttggt cttttttatct tttctttctt tttctttctt    2160

ttcttttttt ctttttttttc ttttttttttt ttttgcttc cacaggttgc actattgaaa    2220

aatcgagatt gtataaacct ggtaaaaagc tgcaagatgc caaaatcttg tagatgtcaa    2280

ataaaaagtt attatact                                                   2298
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<210>    526
<211>    618
<212>    DNA
<213>    Homo sapiens

<400>    526
cttttgcggg tggcggcgaa cgcggagagc acgccatgaa ggcctcgggc acgctacgag    60

agtacaaggt agtgggtcgc tgcctgccca cccccaaatg ccacacgccg ccctctacc    120

gcatgcgaat ctttgcgcct aatcatgtcg tcgccaagtc ccgcttctgg tactttgtat    180

ctcagttaaa gaagatgaag aagtcttcag gggagattgt ctactgtggg caggtgtttg    240

agaagtcccc cctgcgggtg aagaacttcg ggatctggct gcgctatgac tcccggagcg    300
```

```
gcacccacaa catgtaccgg gaataccggg acctgaccac cgcaggcgct gtcacccagt   360

gctaccgaga catgggtgcc cggcaccgcg cccgagccca ctccattcag atcatgaagg   420

tggaggagat cgcggccagc aagtgccgcc ggccggctgt caagcagttc cacgactcca   480

agatcaagtt cccgctgccc caccgggtcc tgcgccgtca gcacaagcca cgcttcacca   540

ccaagaggcc caacaccttc ttctaggtgc agggccctcg tccgggtgtg ccccaaataa   600

actcaggaac gccccggt                                                  618
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<210>  527
<211>  2640
<212>  DNA
<213>  Homo sapiens

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gggaatttta ccaggtcgtg cacacacaca agccgcactt catggccttg cactgtcagg   120

agtttggagg gaagaactac gaggcctcca tgtcccacgt ggacaagttc gtcaaagaac   180

tattgtcgag tgatgcgatg aaagaatata acagggctcg agtctacctg gatgaaaact   240

acaaatccca ggagcacttc acggcactag gaagctttta ttttcttcat gagtccttaa   300

aaaacatcta ccagtttgac tttaaagcta agaagtatag aaaggtcgct ggcaaagaga   360

tctactcgga taccttagag agcacgccca tgctggagaa ggagaagttt cgcagactac   420

ttccccgagt gcaaatggtc aagaaaaggc ttcatccgga cgaggtggtg attgcagact   480

gtgcctttga cttggtgaat atccatcttt tccatgatgc ttccaatctg tcgcctggg   540

aaacaagccc ttccgtgtac tcgggaatcc ggcacaaggc actgggctac gtgctggaca   600

gaatcattga tcagcgattc gagaaggttt cctactttgt atttggtgat ttcaacttcc   660

ggctggattc caagtctgtc gtggagacgc tctcagcaaa accaccgatg cagacggtcc   720

gggccgccga caccaatgaa gtggtgaagc tcatatttcg tgagtcggac aacgaccgga   780

aggttatgct ccagttagaa aagaaactct cgactactt caaccaggag gttttccgag   840

acaacaacgg caccgcgctc ttggagtttg acaaggagtt gtctgtcttt aaggacagac   900

tgtatgaact ggacatctcg ttccctccca gctacccgta cagtgaggac gcccgccagg   960

gtgagcagta catgaacacc cggtgcccag cctggtgtga ccgcatcctc atgtccccgt  1020

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ttgggcccaa cgtctgcatg ggagaccaca gcccgtgtt cctggccttc cgaatcatgc  1140

ccggggcagg taaacctcat gcccatgtgc acaagtgttg tgtcgtgcag tgacgtggtg  1200

ggaagagatg ccagcgccac gagaggacac ttcgtgagcc tccctgtagc cgtggaccga  1260
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273

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atacgcactc ttgaaagctg catcgagaac ccgcccaagc gccacctgct agacggccag    1320

ccccacactt cgcttcagcc tccggaccat tccggagcag ccccacatac ctcactgtct    1380

cgtctgtcta tgtgacatta agtagaaata ttggtttttt ttttttttta aataagtcac    1440

agtcctgttg tcaaaactct aatagacagc aaagagggtc tgtaccgtag acttcacagt    1500

tttcagtttt taatgattgc cagtggaggg gcttcttcag cacagagacc ccccactgtg    1560

tccagggacc ccctctgcca ggtggaggtg tgtccagggg ctggggaagc cgagacgggc    1620

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tgctccttcc gcggcactga ctctgcgccg tgtcacatgg tttttgaatc acactgcagc    1740

tgctttccat ttttatatat atataaatat atataaatat atacttttta aaaataattt    1800

ataaatctta ccaaaactta tgctaaatat actttccagt atgaacgcac aggagagtcc    1860

catcagcagg cggcattgga gtctaggagc tcagctgtgt gtccatcaac acacaaattc    1920

gtaaaaaaca cacatggcct cgccatcgtg ggtaaaatcg gccccacagc acgtctgcac    1980

cagcgggccg ttactcccat gccgttcttc tgtgtaatat taagaactga atgtgaagtt    2040

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agcctagttt gcttccaata gaaactgctt ttaacatggg ctgtatataa aaatattaaa    2220

gagaaacaaa actgtacatt tcctcattgc tccgctacag acaacccatg tcataacctt    2280

gttgcaaata tttttctcct atagcagtaa gtacagcatt agaaggtgat tagagagtct    2340

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ggttgccgct gtccgcggtt caacacggag tccgccccgc gggtttcagc tgttggtcgt    2580

tctgaggggc ctttggaagt gaccggtctg gttcctaagc aataaaattg accgtggtga    2640
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<211>  743
<212>  DNA
<213>  Homo sapiens

<400>  528
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caacttgttc aagagaaggt cttgtacgtg cctaagttct agagcctcct gacgtgagca     120

tggctgagag tgaggaccgc tccctgagga tcgttctggt agggaaaact ggaagtggga     180

aaagtgcaac agcgaacacc atccttggag aggaaatctt tgattctaga attgctgccc     240
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aagctgttac caagaactgt caaaaagcat cccgggaatg gcaggggaga gaccttcttg    300

ttgtagacac tccagggctc tttgacacca aggagagcct ggacaccacc tgcaaggaaa    360

tcagccgctg catcatctcc tcctgcccag ggccccatgc tattgtccta gttctgctgc    420

tgggccgcta cacagaggag gagcagaaaa ccgttgcatt gatcaaggct gtctttggga    480

agtcagccat gaagcacatg gtcatcttgt tcactcgcaa agaagagttg gagggccaga    540

gcttccatga cttcatagca gatgcggatg tgggcctaaa aagcatcgtc aaggagtgcg    600

ggaaccgctg ctgtgccttt agcaacagca agaaaaccag taaggcagag aacgaaagtc    660

aagtgcagcg agttgggtgg aagctgatag agcaacacat ggtgcagtgc aacgaacggg    720

ccttactttt ctgatgacct ata                                            743
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<210>  529
<211>  346
<212>  DNA
<213>  Homo sapiens

<400>  529
cttttacctc gttgcactgc tgagagcaag atgggtcacc agcagctgta ctggagccac     60

ccgcgaaaat tcggccaggg ttctcgctct tgtcgtgtct gttcaaaccg gcacggtctg    120

atccggaaat atggcctcaa tatgtgccgc cagtgtttcc gtcagtacgc gaaggatatc    180

ggtttcatta agttggacta aatgctcttc cttcagagga ttatccgggg catctactca    240

atgaaaaacc atgataattc tttgtatata aaataaacat ttgaaaaaaa aaaaaaaaaa    300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa                   346
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<210>  530
<211>  397
<212>  DNA
<213>  Homo sapiens

<400>  530
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ccaaacagtt caacctacac gaacaggcaa ccatgcctgg tgtatttatt aaaatgtagc    120

tactagaata tttaaaattc acatgtgcct cacatattat ttcttagaga attgcctcat    180

ttttgaaatc tcaggctgcc tgctctaaaa cctggatgtg ccaggaaagt aaaaaatctg    240

aaattttaaa ataattgtca ttatattgct tccatgtatg aataacacat atatatttt     300

cataaataca aataatctta cacacaaatg aaaatgcaag tattttacag tcagggccag    360

tgtccagtgc atgaaggaag ccctgccaga aaaggat                             397
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<210>  531
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<211> 1236
<212> DNA
<213> Homo sapiens

<400> 531

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caggtcttcg ggaggggtct cggtgggctg ctcaaactgc cccacggcgt aggccttcgc     120

ggccgtctcg tagataggca gcatgaaccc accctggttg gtggagaaga tgcgcaccat     180

gacctgtttg ggaaactttt gcatcagggg caggcacagg ttgagagcgc caacaggtc     240

cacgggggtg gcagcgtgga tgatcatgtt gcggtaatcg gaggaacggg ggcataattg     300

gtgggtgtgc aattctttga ggctccacgc ggccttgacg ccttcgttac aagcatcggc     360

tgtgcgctgc gccacttcgg gtggatgtgt cacgggcatg gtgtgctcca tgaggaaggg     420

agtggagagg gccaggttgc acatggtgcc caggcgacac cgcaccgcat ccacctcact     480

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cgaagaggaa ctatcttcat cgggccggcc caagggatcg ggaagaggag ggtggttcat    1020

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agacgcggta gcaccgcggg tttcgacttc ttcaccctgt tcttcctcgc tatcagagat    1140

cacgatacag ccggcggtat cgataatctt gttgcggtac tggatggtaa agtcgggctc    1200

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<210> 532
<211> 2034
<212> DNA
<213> Homo sapiens

<400> 532

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aaaccttggc catggtcact tcctctttc caatctctgt ggcagttttt gccctaataa      60

ccctgcaggt tggtactcag gacagtttta tagctgcagt gtatgaacat gctgtcattt     120

tgccaaataa aacagaaaca ccagtttctc aggaggatgc cttgaatctc atgaacgaga     180

atatagacat tctggagaca gcgatcaagc aggcagctga gcagggtgct cgaatcattg     240
```

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tgactccaga agatgcactt tatggatgga aatttaccag ggaaactgtt ttcccttatc    300

tggaggatat cccagaccct caggtgaact ggattccgtg tcaagacccc cacagatttg    360

gtcacacacc agtacaagca agactcagct gcctggccaa ggacaactct atctatgtct    420

tggcaaattt gggggacaaa aagccatgta attcccgtga ctccacatgt cctcctaatg    480

gctactttca atacaatacc aatgtggtgt ataatacaga aggaaaactc gtggcacgtt    540

accataagta ccacctgtac tctgagcctc agtttaatgt ccctgaaaag ccggagttgg    600

tgactttcaa caccgcattt ggaaggtttg gcattttcac gtgctttgat atattcttct    660

atgatcctgg tgttaccctg gtgaaagatt tccatgtgga caccatactg tttcccacag    720

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gaatgggagt taatcttctt gtggccaaca cacatcatgt cagcctaaat atgacaggaa    840

gtggtattta tgcaccaaat ggtcccaaag tgtatcatta tgacatgaag acagagttgg    900

gaaaacttct cctttcagag gtggattcac atcccctatc ctcgcttgcc tacccaacag    960

ctgttaattg gaatgcctac gccaccacca tcaaaccatt tccagtacag aaaaacactt   1020

tcaggggatt tatttccagg gatgggttca acttcacaga actttttgaa aatgcaggaa   1080

accttacagt ctgtcaaaag gagctttgct gtcatttaag ctacagaatg ttacaaaaag   1140

aagagaatga agtatacgtt ctaggagctt ttacaggatt acatggccga aggagaagag   1200

agtactggca ggtctgcaca atgctgaagt gcaaaactac taatttgaca acttgtggac   1260

ggccagtaga aactgcttct acaagatttg aaatgttctc cctcagtggc acatttggaa   1320

cagagtatgt ttttcctgaa gtgctactta ccgaaattca tctgtcacct ggaaaatttg   1380

aggtgctgaa agatgggcgt ttggtaaaca agaatggatc atctgggcct atactaacag   1440

tgtcactctt tgggaggtgg tacacaaagg actcacttta cagctcatgt gggaccagca   1500

attcagcaat aacttacctg ctaatattca tattattaat gatcatagct ttgcaaaata   1560

ttgtaatgtt atagggcgtc tctttatcac tcagcttctg catcatatgc ttggctgaat   1620

gtgtttatcg gcttcccaag tttactaaga aactttgaag ggctatttca gtagtataga   1680

ccagtgagtc ctaaatattt tttctcatca ataattattt tttaagtatt atgataatgt   1740

tgtccatttt tttggctact ctgaaatgtt gcagtgtgga acaatggaaa gagcctgggt   1800

gtttgggtca gataaatgaa gatcaaactc cagctccagc ctcatttgct tgagactttg   1860

tgtgtatggg ggacttgtat gtatgggagt gaggagtttc agggccattg caaacatagc   1920

tgtgcccttg aagagaatag taatgatggg aatttagagg tttatgactg aattcccttt   1980

gacattaaag actatttgaa ttcaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa         2034
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<210> 533
<211> 4500
<212> DNA
<213> Homo sapiens

<400> 533
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gcctaactag caataaaagc aaggatgacc tggtggtagc tgaagtagaa attaatgatg     360

tgcctctcac atgtaggaac ttgctgactc gaggacagac tcaagacgag atcagccgac     420

ttagtggggc tgcagtatca actcgaggga ggttcatgac aactgaggaa aaagccaaag     480

tgggaccagg ggatcgtcca ttatatcttc atgttcaggg ccagacacgg gaattagtgg     540

acagagctgt aaaccggatc aaagaaatta tcaccaatgg agtggtaaaa gctgccacag     600

gaacaagtcc aacttttaat ggtgcaacag taactgtcta tcaccagcca gcacccatcg     660

ctcagttgtc tccagctgtt agccagaagc ctcccttcca gtcaggatg cattatgttc     720

aagataaatt atttgtgggt ctagaacatg ctgtacccac ttttaatgtc aaggagaagg     780

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278

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cgtgtgatct tcaacgtttt tgggtgacca ttgaccctgt gacctcaaaa tggtgtccaa   3120

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agaggaggaa catggaggtc ataaaaatgc aagtagtttt ccacagggct ggagtttggg   3360

ataccaatat ccttcatcac aaccacgagc taaacaacag atgccattct ggatggctcc   3420

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279

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ctgcagtggc atagaatctg ttaaaattta attagaatca caaatttatc tcagaagctt    3660

tttaacagtt ggtgaaatgt gcttgtccaa caaagcatcc taacagggtc gttcccatac    3720

acatttgacc tggtcagcct tttccaggtg aatagcccca gttctgacat aaagaaagtt    3780

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gcaaattgtc ctttttcttg gcattacaga ttttgccaaa ataacttttt gtatcaaata    4320

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tgtcattttt gcacatttga atactttgca ggctggcttt gtataaactt atcctctggt    4440

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<213> Homo sapiens

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<223> n is a, c, g, t or u

<400> 534
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cttgctctgg tttctgggtc taacaattac gacttaaaca atggagccaa agaaaaatac    180

attagatgat tctcaacctg gaaagcaaga ctgcaaatta taaccacaaa aacaaagatc    240

tactgtctcc cagataccgg aaatggtaac ccggatattt gaggcttcca aggcaggaag    300

ataaaggaga atcagacccc tgagcaggga ctctggagca gcactccagg accctgccta    360

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agatgtacac agattggggt gttgggtgag ggcctgatgg gggaaaggaa agagagaact      480

gctataggtg aatctctctg tggcttgttg tgggaccctg cgccctttaa attagggcat      540

attttacaaa aacttattat tctacacagc ccttcttggg cctttacaga acga            594
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<210> 535
<211> 1721
<212> DNA
<213> Homo sapiens

<400> 535

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cactactggg gacctaagct ggttctcaaa tgcctctcct tttcccctcc aagcctccca      180

ggcttcctat ggtccctaag tcccgggttc tcagcgtgac attccagagc aaacacagct      240

ccccattact ctataccagg cactggcatg gattaattta tctaatcaca acatcccagt      300

aagatatgcc ctgcctctcc tgctcacact ctatggctgg cattcacctg tggggccagg      360

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ccgggaccct gactactctg tgtcctgcct ctactcacct ccctcaccct ccagcatgtg      600

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tctatcagaa gctccaagcg caggaggatg agatctcaga gaacttggtg aacattcaga     1380

aaatgcagaa aacgcaggtg aaatgccgca aaatcctgac caagatgaag cagcagggtc     1440
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281

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atgagacagc cgcctgtccg gagactgaag agataccgca gggagccagt ggctgctgga    1500

aggatgacct ccagaaggaa ctgagtgata tatggtctgc tgtgcacgtg ctgcagaact    1560

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acaaggggca ccagtgcctg agccctccac tcccctcctg ggactctgac tccgactgtg    1680

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<210> 536
<211> 526
<212> DNA
<213> Homo sapiens

<400> 536
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ctttgctgcc agaaaagaca aaaagcacaa ataaacaagc acctgacagc gttataggtg    180

gagaccgagt tctatgagtg cagtaaagtg gggcacggca cagagatgga gctgtactct    240

agacagggtg ttctgaatca ggaatggact tacaaaacat ctgcagtcag aaattcacat    300

acagactata gtagatcaaa agctcatttt aaactatcaa tgaggaaaaa agcaattcat    360

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gccagaaatc tgtcattaca caatagctta gcaagtgtga cacaagatac tgccactttc    480

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<210> 537
<211> 1837
<212> DNA
<213> Homo sapiens

<400> 537
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agtccaccac tactggccat ctgatctata aatgcggtgg catcgacaaa agaaccattg    180

aaaaatttga gaaggaggct gctgagatgg gaaagggctc cttcaagtat gcctgggtct    240

tggataaact gaaagctgag cgtgaacgtg gtatcaccat tgatatctcc ttgtggaaat    300

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cttacacact gggtgtgaaa caactaattg tcggtgttaa caaaatggat tccactgagc    540
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atggcaatgc cagtggaacc acgctgcttg aggctctgga ctgcatccta ccaccaactc     780

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tggaaacaac ttgaccaaaa atttgtcaca gaattttgag acccattaaa aaagttaaat    1740

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa                             1837
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<211>   1697
<212>   DNA
<213>   Homo sapiens

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ggagcaaact atcgctgagg acctggtcgt gaccaagtat aagatggggg gcgacatcgc     180

caacagggta cttcggtcct tggtggaagc atctagctca ggtgtgtcgg tactcagcct     240

gtgtgagaaa ggtgatgcca tgattatgga agaaacaggg aaaatcttca agaaagaaaa     300
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cgcctggtca ccagggctgc tttttaactct ggtaaagtgg atattgttgc catcaatgac   180
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<211> 6417
<212> DNA
<213> Homo sapiens

<400> 540
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cccacccaga aaatgaagag gacccagaag aggatttgtc agaaacagag actccaaagc    240

tcaagaagaa gaaaaagcct aagaaacctc gggaccctaa aatccctaag agcaagcgcc    300

aaaaaaagga gcgtatgctc ttatgccggc agctggggga cagctctggg gaggggccag    360

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ctcctggcaa gaagaagaag aagaagcttg gacctaagaa agagaagaag agcaaatcca    480
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agcggaagga ggaggaggag gaggatgatg atgatgatga ttcaaaggag cctaaatcat    540

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<213> Homo sapiens

<400> 544

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294

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actgggaatt tccctgtggg caaaatacag gggaggtgtg tagctttca tcttgtagcc     1860

atcctattta gaaaccaaaa gggggggagac aggtttgcat gacccagttc ccagcttgac    1920

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catctcgcca acttcagagc cgaatggcct ctagccacac tgcttccaga ccccagacgg     360

ggcagcagca gcagttccca gatgagcacc cattgttgca gctaggaccc accaaggatg     420

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<213>    Homo sapiens

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gacaggaaat tcattgttgc ttgataaatg tcctctccaa gtcaccccat cttgggaaac     240

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ttctgtcact ctgtctcccc aaccccaatc cagctcatca gcaagtcccc caagcctggc     360
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<213>  Homo sapiens

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aaagggaat ttccatgccg tctacaggga tgacctgaag aaattgctag agaccgagtg         180

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ccacaaaaaa agccatgaag aaagccacaa agagtagctg agttactggg cccagaggct        360

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aaaaaaaa                                                                428
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acattgaaat gacaagagga aactcttaaa tacataaaaa caagctctca tttgcctagg        240

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<213>  Homo sapiens

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taggacgcag ccgcctcatg ggggtccagg ggctctggaa gctgctggag tgctccgggc      240

ggcaggtcag ccccgaagcg ctggaaggga agatcctggc tgttgatatt agcatttggt      300

taaaccaagc acttaaagga gtccgggatc gccatgggaa ctcaatagaa aatcctcatc      360

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tgtttgatgg ggatgctcca ctattgaaga aacagacttt ggtgaagaga aggcagagaa      480

aggacttagc gtccagtgac tccaggaaaa cgacagagaa gcttctgaaa acatttttga      540

aaagacaagc catcaaaact gccttcagaa gcaaaagaga tgaagcacta cccagtctta      600

cccaagttcg aagagaaaac gacctctatg ttttgcctcc tttacaagag gaagaaaaac      660

acagttcaga agaggaagat gaaaaagaat ggcaagaaag aatgaatcaa aaacaagcat      720

tacaggaaga gttctttcat aatcctcaag cgatagatat tgagtctgag gacttcagca      780

gcctgccccc tgaagtaaag catgaaatct tgactgatat gaaagagttc accaagcgca      840
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298

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cctacctcaa acccgtggtg gatgactcga agggatcctt tctgtggggg aaacctgatc    3060

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<210> 550
<211> 344
<212> DNA
<213> Homo sapiens

<400> 550

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attcctactt catggatgtg aaatgcccag gatgctataa aatcaccacg gtctttagcc     180

atgcacaaac ggtagttttg tgtgttggct gctccactgt cctctgccag cctacaggag     240

gaaaagcaag gcttacagaa ggatgttcct tcaggaggaa gcagcactaa aagcactctg     300

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<212>   DNA
<213>   Homo sapiens

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<210> 552
<211> 390
<212> DNA
<213> Homo sapiens

<400> 552
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gcaggaagga gaggaaaaga aaaaaagaca aagaggagat gagagaaaaa aatccagttc   180

agcacaacaa aagtgcaaaa gctcacctac ccaaatggca ttaaagcctc gttgtgtaat   240

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302

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308

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aactcaaatt ccctgagcct caagaggtgg tggaagagtt gaacgcaagt acctgtcgat    420
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cctggattgg ggtttactac caccgtttga cacttacggt acacacaaac acacaaaaaa     660

aaacgttggg gggcactcta tagtgccgag gggcgcggac aacaccgcgg ttacatgaac     720

gtggcacatt ggggccaata gggtgttccc ctggacgcac agtttctttg gtacacaggg     780

tggggtaaac tctggcgggg acacccctta atagggagag ggcgagaata aattttcgga     840

taaacgcagg gttaccttgt atagacatct tgactgtaca acaagagggg aacgaaaacg     900

aaagcacaaa acaaaggaga aaaacgacga ctgggagaaa aggaggagga gagggaggag     960

gagagggaga gcagaagaag cgagaggagc aggaaaagag gaggaccacc caaagagacg    1020

aggaaacaag agaggagaga gaacagagga taacgcgaaa gaaaggaaga agcacgatgc    1080

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<213>  Homo sapiens

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tcaagtccca gcagagcgag gtgacccgaa tcctggatgg gaagcgcatc caataccagc     180

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tcgtggaggc tgtggaacaa aacacgctgc aggagttcct gaagctggct tgagtcaagc     360

ctgtccagag ttccctgct ggactccatc accacactcc ccccagcctt cacctggcca     420

tgaaggacct tttgaccaac tccctgtcat tcctaaccta acttagagt ccctcccccc     480

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gcaacattcc ttacccatta gtctcagaaa ttgtcttaag caacagcccc aaatgctggc     600

tgcccccagc caagcattgg ggccgccatc ctgcctggca ctggctgatg ggcacctctg     660

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<210> 562
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<212> DNA
<213> Homo sapiens

<400> 562

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tgctgctctg ggcggccgcc gcctccgccc agggccacct aaggagcgga ccccgcatct  180

tcgccgtctg gaaaggccat gtagggcagg accgggtgga ctttggccag actgagccgc  240

acacggtgct tttccacgag ccaggcagct cctctgtgtg ggtgggagga cgtggcaagg  300

tctacctctt tgacttcccc gagggcaaga acgcatctgt gcgcacggtg aatatcggct  360

ccacaaaggg gtcctgtctg ataagcgggg actgcgagaa ctacatcact ctcctggaga  420

ggcggagtga ggggctgctg gcctgtggca ccaacgcccg gcaccccagc tgctggaacc  480

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actgcatcct gttcatcgag aacctcacgg cgcagcagta cggccactac ttctgcgagg      1860

cccaggaggg ctcctacttc cgcgaggctc agcactggca gctgctgccc gaggacggca      1920

tcatggccga gcacctgctg ggtcatgcct gtgccctggc cgcctccctc tggctggggg      1980

tgctgcccac actcactctt ggcttgctgg tccactaggg cctcccgagg ctgggcatgc      2040

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<213>   Homo sapiens

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tcctggctgc gcattggctg cgaaggccgt cagtactccg gagggcggag cctcccggca      180

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aacggttcct ttgccttttt atttcgcagg ccttcctctc acccatacag ttactgccc       360

ctttgactcc tccgagaggc aaagcttttt caaagctcta acacctctcc cctaccccag      420

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<211> 430
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tccttaatgc aacatctcct gagggcctac tttgtgtcag aaactacatt atttgctagg     180

ggtgcagagc ccaggaaggc acaggtgctt ccctcaagca gttctgaaat gaatagggta     240

cagataagta aacccccctc tcctatccag tgagtagagt tgtgtacaag gggacacaaa     300

atgagctctg gagacttgct cccccaaaat gggagccatg gaccatcagc attggcatca     360

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caaatcaagc tcccaaggtc aagatcgcca catgattaga atgcgtcaac ttatagatat     180

tgttgatcag ctgaaaaatt atgtgaatga cttggtccct gaatttctgc cagctccaga     240

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gtcagcaaat acaggaaaca atgaaaggat aatcaatgta tcaattaaaa agctgaagag     360

gaaaccacct tccacaaatg cagggagaag acagaaacac agactaacat gcccttcatg     420

tgattcttat gagaaaaaac cacccaaaga attcctagaa agattcaaat cacttctcca     480

aaagatgatt catcagcatc tgtcctctag aacacacgga agtgaagatt cctgaggatc     540

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<212> DNA
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gttatttgag aagttaatga actctcagca ctccatgatt ctagaacaga ttttgaacag    1620

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aatctattta atactacctg agtttcccct actccaggat tccaagtatt atataacatt    1740

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314

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agactacctc atgtggttct tgcatcaagc agggatgaag gctagaccat caataataca     2100

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aagtatggag gtaggaagac accatatgtc caggatcaaa acattcctca tattgaggta      180

gtctagtgaa gctgtttcat gtagctgctt taggaagtgg tttaaggaag cttactccca      240

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<212> DNA
<213> Homo sapiens

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tgagaagctg ttctccaagc ccacctatgc agccttcatc aacctcctca caactacca     660

gcgggcaaca ggccatgggg agcacttcag tgcccaggag ctggccgagc aggacgcctt     720

cctcagagag atcatgaaga cagcagtcat gaaggagctc tacagcttcc tccatcacca     780

gaatcgctat ggctcagagc aagagtttgt cgatgacttg aagaacatgt ggtttgggct     840

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agaagcattc ctaaatccca aagtgcccac atgggaaaga gataaaatgt acaaattaga    1440

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acagagtcca agcagagaag gtaggaaccc tccatagctc tctgccctga tgtgtggggg    1560

aactaggaag aagtcctttg acctcaccag gcctcatgct tcccttttaat gtaaagggaa    1620

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aacatgtttc  tttcttggtc  tctggttatc  ccacctgagg  agagaggcct  ctgatgacca      180

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gagctgatga agagggtgca gcagagctct gggcctgcat gaggtccctg tcagtataca    420

ccctgggggtg taccccaccc cttcccactt taataaacgt gctccctgtt gggtgtcatc    480

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gccctgttg tcattcaaat gtgtacctct acagttgtaa aaagtattag attctactat     3600

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agaaggagaa cagccacttt ttcgtcgcca cctttgctcg ggagcgagcg gccgtggaag     240

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ggctgcagaa actaatcaac gactcagttt ttttcctagc cgcttacgac ctgcggcagg     360

gacaagaggc gctggcgcgg ctgcaggcgg ccttggccga gcggcgccgg gggctgcagc     420

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321

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<213> Homo sapiens

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gcggaggaga agccggagga ggacaacgac taccaccgca gcgacgagca ggtgagcatc      600
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<213>    Homo sapiens

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gaagatgtga tgcaaccatt ttgtatagct gtagtaggga ggcattgcaa aagctcattg     180

acgatcaaga tatcagtatt tccttattgt ctttgagaat cctgtcattt cacaataaca     240

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ggaaagctgc cttattctct ttttgcagta aagtatgttg ttttcattgt aaagatgttg    1560

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<212> DNA
<213> Homo sapiens

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<213>   Homo sapiens

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gccaagctct cctgccctgc cctcggtatc tctaagagga acctctatga ctttgaagtc   180

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<213>  Homo sapiens

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acggatttta atgaataata tagttatccc ggataccatg ctggcaggat ccactttgcg      660

aaattgtgga ctgttggact gtgattctaa gtgggggaaa taggctttag                710
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<213> Homo sapiens

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<400> 579
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ccagtcgaac tggtaagcct cgcccggctc aaagctcagc ggcacgaacg cggtcgccgt      180

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<211> 2693
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<213> Homo sapiens

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tgcagtaaag atgttggtgt cattaaaaat gagctacaaa gctgccgcgg gggaggatta      360

caaggctgac tgtcctccag ggaacccagc acctaccagt aatcatggcc cagatgccac      420

agaagctgaa gaggattttg tggacccatg gacagtacag acaagcagtg caaaaggcat      480

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ccgaatagag agagccaccg gccaaagacc acaccacttc ctgcgcagag gcatcttctt      600

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333

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acactgatat gcattttgaa atatgtagtt aattctcaat tttattgcag aattctgcaa    180

acagtggtta acattgctta cagattttct gcatgttaat ttgaatcttt aatcatatta    240

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agtcatactg tagactcatt aaaaccaggg ttcaaggact cacctaagtg cagccaagct    240

ggaagaattc attccgagtt tggtgtcgaa ttctctcaaa tcaaccagcc agactctaac    300

tgtaccctca gcattgccaa caggctctac gggacaaaga cgatggcatt tcatcagcaa    360

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tcaccaacca agggcctata tttatcaaaa gccatccaca agtcatacct ggatgtcagc     1020

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attctgatta taagtagtgg ctcttgacta caatcaagtc tcaaataata gtgtaagaga      180

ataaagcaga ataataagac taagttaaca gtttaggctt ctttggaatc atgcgggcct      240

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ctttgatgcc tcagttttct cctctgtgtt gtggggtaat agtaatatct acttcctggg      360

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tgttatttcc ttggccaaac tttcttactc tgccatttgt tcaatgtcct aatgagcatg      480

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aacctaaaat ctgggctcct aaataccaag cttcactggc tctctggtcc cagtgagagt      720

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338

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340

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gttagtgtag gtgtgttgcg tcatctgttt tcaaccagat tgcatttatg gacttttcac   1920

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gcagaggtct ctgtattttg cagctgccct tttgtaagaa gcacttttcc caaataaaac    3060

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<212> DNA
<213> Homo sapiens

<400> 590
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gccgcgcacg ctacagtaca agctgctgga gccagttctg cttctcggca aggagcgatt    240

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343

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345

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<213>  Homo sapiens

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aggataatgt cctacaaaaa cgtgagtaca agcaagcaaa gacatttgca gaaagatttt   420

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ctgtgactta ctcgaagcct cgattggcca catttttggta ctacgccaag gttgagctgg   180

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gtgctcagac tggtagcttc aaacagctca cagttaagga agctgtgctg aatggtttgg   300
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gcaaaaacaa aataccccaa agatatttaa acaaggttat aatttagcat cttccctgga       1080

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<212> DNA
<213> Homo sapiens

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<400> 596
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aatttccaat agtccgtgaa agttggggct gaagtaccta agtgtgaatg tctctcccgt    1860

taaactgagt gtagaaatct gaatttttaa aagagctgta actagttgta agtgcttagg    1920

aagaaacttt gcaaacattt aatgaggata cactgttcat ttttaaaatt ccttcacact    1980

gtaatttaat gtgttttata ttcttttgta gtaaaacaac ataactcaga tttctacagg    2040

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<210> 597
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<213> Homo sapiens

<400> 597

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gatattacag ggcaaatgtt cccagacagc ccagcctgct cccccttagga atgagtgtcc    180

ctggaggggg agagcctgga accaaagccc cgccaggaac tgcttcccct aaactgaggt    240

tctctgaaaa aaatgttcgc ctggctgata aagccgcctc ttaacagagc ccagacactt    300

ctgtgcttcc cctgggttgc taattgagga cactaaagcc ctaagagata ccccaggtcg    360

ggggaagggg ccccaagacc tagacctccg gtggcgacca tgcccttgag aggatgggag    420

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<212> DNA
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<400> 598

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350

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gcagcgtgtg tgggaaagtc ttcctccgtc attcattcct ggacaggcac atgagagctc      480

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atatatgtgt atatgtacaa atacatgtat atatagtaca aatatatata tatatttgta      180
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351

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caattcttca gactttgtag aatttgtata atgtcgtatc ttgctttttt taaccactga    240

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tggataattt atcattccct gatggagaaa aatttagctt tgtttatttt agagttataa    360

acgatgctgg gtcaggtatc tttatgtttg aagatggctc catatttggg ttgtttccac    420

agaactcttt cctagaaatg cttttctag gttaatggct acagatattt ctaggcacct    480

gacatattga cacccacctc taaagtattt ttatgatcca caactagcgt ttaacacagc    540

gccctagtca ctacatgact aataaataga caaatgactg aaacatgacc tcatgctttc    600

tattcctcca gctttcattc agttctttgc ctctgggagg aggaagggtt gtgcagccct    660

ccacagcatc agcccatcaa ccctatccct gtggttatag cagctgagga agcagaattg    720

cagctctgtg ggaaggaatg gggctggaga gttcatgcac agaccagttc ttatgagaag    780

ggactgacta agaatagcct tgggttgaca tatacccctc ttcacactca caggagaaac    840

catttcccta tgaaactata acaagtcatg agttgagagc tgagagttag agaatagctc    900

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gctgacacgc cgaccgcctg ctgcttcagc tacacctccc ggcagattcc acagaatttc   1980
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<213>   Homo sapiens

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agagcgaata   130

<210>   601
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<213>   Homo sapiens

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<210> 602
<211> 921
<212> DNA
<213> Homo sapiens

<400> 602
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ggtatcggtc gccgaccact ccctgcacct aagcaaagcg aagatttcca gccagcgcc     300

ctactgggaa ggaacagctg tgatcgatgg agaatttaag gagctgaagt taactgatta    360

tcgtgggaaa tacttggttt cttcttcta cccacttgat ttcacatttg tgtgtccaac     420

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<210> 603
<211> 2591
<212> DNA
<213> Homo sapiens

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ggagagcatc tttctgaagc gatcccaaca gaaaaagaaa acatcacctc taaacttcaa    240
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gaagcgcctg tttctcttga ccgtgcacaa actctcctac tatgagtatg actttgaacg    300

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agtggttcct gaaaaaaatc ctcctccaga aagacagatt ccgagaagag gtgaagagtc    420

cagtgaaatg gagcaaattt caatcattga aaggttccct tatcccttcc aggttgtata    480

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aaaaaaaaaa a                                                          2591
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<212> DNA
<213> Homo sapiens

<220>
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<400> 604
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caaaactgag ccaatcccac ttaggaatgg aaggcttgga catggaaggg aggatataaa       180

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<210> 605
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<213> Homo sapiens

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tcaagattcc cactccccag aggtgaccac tttcaactct tgagttttc aggtatatac    2100

ctccatgttt ctaagtaata tgcttatatt gttcacttcc ttttttttta ttttttaaag    2160

aaatctattt cataccatgg aggaaggctc tgttccacat atatttccac ttcttcattc    2220

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atgtacctgg gttcgctcgc cttcctaggc gctgacaccg ctcggttgga tgtcgcgtcg    240

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ccgcgtggaa tgtgagtgtg tttgtgtgca tgaaagagaa agactgatta cctcctgtgt      1380

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aagttgaata tgttaaggaa taagaattaa tctcatttaa agcctcaaaa caaccatgaa       360

aaggattaga aacattttan nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn       420

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aagaagttca agttgaacta tgccgtggat aaaagagggc gccccattag ccatagcact    300

acagaggatt tgaagcgttt ttacgacctt tcagattctg attccaatct ctctggtgaa    360

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atcgattcaa aaatctagt tgagaaaaag aaagaaacca agaaggctaa tcacaagggt     480

tctgaaaata aaactgattt agataattct ataggaatta aaaaaatgaa aacctcatgt    540

aaatttaaga tagattcaaa cataagtccg aagaaggata gcaaagaatt tacacaaaaa    600

aataagaaag agaaaaaaaa cattgttcaa catactacag actcttctct cgaagaaaaa    660

caaaggacat tagactcagg cacctctgaa attgtgaaat ctcccagaat cgagtgttct    720

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gcttcaggtg atgacgatgg aagtgaagat gatgaagagg aggatgaaga tgaagaggag    960

gatgaagatg aggatagtga ggatgatgat aaaagtgaca gtggccctga tcttgcaagg   1020

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gttgatttga atgacccata ctttgctgaa gaagttaaac aaataggtat aaataaaaaa      2160

tcggtaaaat ctgcaaaaga tggcacatct ccagaagaag aaattgaaat agaaagacaa      2220

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gtccaaatca  tgaaatgttt  ggccttagtc  aatgtctatg  cccgtcacat  aacagccgag      1560

gcaccgaggc  ccacagggaa  gcagctggga  gcttggaaac  ctggtctctt  gaatttcaaa      1620

cctggtttct  tacaggtggt  tgtctggggt  gggtggagtg  gcgacaggat  agagctgaag      1680

gactatgcaa  atgaggaagt  aagtcagggc  gggctttgag  aaggggaccc  atatcctaca      1740

ggcaaaaagc  aggctaggtg  accttgggac  actacgctaa  gggagggagg  ctaaaggcgg      1800

ccaggtttgc  agtgcgggaa  gatgagcagg  ccagtgggag  gaggggcagg  gcagggctgt      1860

agttggtgac  tgggtgttca  ttttagctct  aagaaaaaaa  atcagtgttt  cgtgaaggtg      1920

ttggagaggg  gctgtgtctg  ggtgagggat  ggcggggtac  tgatttttt   gggaggttat      1980

gagcaaaaat  aaaacgaaac  atttcctctg                                         2010
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<210>  613
<211>  1263
<212>  DNA
<213>  Homo sapiens

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cgctatgtgc  ctctgccatc  ttcacccatc  atggagcaga  ggtgaggaga  ggcagcctgg       180

gaatatggag  accagtgaag  gaccaggcct  ggagagcaca  gggtcctacc  tgggcatcca       240

gcagaggagc  ccctaaaggc  caggagcacc  ccaagaggag  ggaggcagc   cagcctccat       300

tgacggcgag  cctccagccc  tctcctactt  tgatcaccat  ttctctccag  gctttctgcc       360

tccgagatgt  ggcaccatag  tgcggtgccc  tgtggcttca  ccgccctact  tccacctccg       420

cccagcctgt  aatgtttata  taagcagcct  caaggaccaa  gaaccatctg  cgaaaggaca       480
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cacacaggaa attcataaaa gaaatctgaa tggataaaac catgaaaaaa agtatgcttc      540

attagtaatt aaagaaaggc aaatagagct ggaagcattt ttcccttagc aaaccataac      600

agaaaaaaat aagacccaat attggcaaag agactactga aaaaacattc ccatacattg      660

cgtgtgggag tatacatcgg tgcaggcttc ctggatgaca gttgggtgat atgtgtcatg      720

tggcctaaaa gcctccatgt catttgacct acgaattcta tctttgggaa tttatcctaa      780

gaaaatactt aaggatttag ttagtgataa gatgttcatc ccagcattgc aatggagaaa      840

aatgggaagc aatggtttgg ttgggaattt attccttttc tgctgtaacg aaagtttgca      900

atagggggatt gcttaagtaa attattgtat ctccatccag atggtggagt accgcgcaga      960

cattaaaagt catgtaaaag aacatctgac tgaaagaaaa atgctccttg aatattaaaa     1020

ggttgtaaaa atagtgcatg ttatgtgatt tcaattttgt tttttaaaat atgggtgtat     1080

gcttgtatac gtagagcaga taaaaaagac ggaaggcata ctaaaaaatg ttgagtggtt     1140

atctttgtat ggtggaacaa agtcactgta attttcatct ttggtttttc tgtaatttcc     1200

aaatttttcca cattttgtat ttcatataat aaatataatt taagaaaaaa aaaaaaaaaa     1260

aaa                                                                    1263
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<211>   447
<212>   DNA
<213>   Homo sapiens

<400>   614
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taaaggtgtg gctttattta cacacactct tgaagctctt ggcattcagc ggacagcaaa       120

caccatactc agagtgatgg aattaatagc atttagggta agcaaggacc agtgtgagac       180

tgggcccagg aaatggggag ggaatgtgag gagaaacagg gaatgacatt aaagaagaaa       240

cagacacctt ggagaattta tgactccttt ctctatgtca tgtccagaag aggcaagtct       300

acagagatca aagtagccta ggggtgccta gggatgggga ggttgggggtg gcgactaagg       360

ggggctggat ttctttttggg ggtagtcaac tctaagacgg actgtgctga tggctgctga       420

actgtgacta tactaaaccg gcatcaa                                           447
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<210>   615
<211>   2372
<212>   DNA
<213>   Homo sapiens

<400>   615
gcaccgcgcg agcttggctg cttctggggc ctgtgtggcc ctgtgtgtcg gaaagatgga        60
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gcaagaagcc gagcccgagg ggcggccgcg acccctctga ccgagatcct gctgctttcg    120

cagccaggag caccgtccct ccccggatta gtgcgtacga gcgcccagtg ccctggcccg    180

gagagtggaa tgatccccga ggcccagggc gtcgtgcttc cgcagtagtc agtccccgtg    240

aaggaaactg gggagtcttg agggacccccc gactccaagc gcgaaaaccc cggatggtga    300

ggagcaggca aatgtgcaat accaacatgt ctgtacctac tgatggtgct gtaaccacct    360

cacagattcc agcttcggaa caagagaccc tggttagacc aaagccattg cttttgaagt    420

tattaaagtc tgttggtgca caaaaagaca cttatactat gaaagaggtt cttttttatc    480

ttggccagta tattatgact aaacgattat atgatgagaa gcaacaacat attgtatatt    540

gttcaaatga tcttctagga gatttgtttg gcgtgccaag cttctctgtg aaagagcaca    600

ggaaaatata taccatgatc tacaggaact ggtagtagt caatcagcag gaatcatcgg    660

actcaggtac atctgtgagt gagaacaggt gtcaccttga aggtgggagt gatcaaaagg    720

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ctacctcatc tagaaggaga gcaattagtg agacagaaga aaattcagat gaattatctg    840

gtgaacgaca aagaaaacgc cacaaatctg atagtatttc cctttccttt gatgaaagcc    900

tggctctgtg tgtaataagg gagatatgtt gtgaaagaag cagtagcagt gaatctacag    960

ggacgccatc gaatccggat cttgatgctg gtgtaagtga acattcaggt gattggttgg   1020

atcaggattc agtttcagat cagtttagtg tagaatttga agttgaatct ctcgactcag   1080

aagattatag ccttagtgaa gaaggacaag aactctcaga tgaagatgat gaggtatatc   1140

aagttactgt gtatcaggca ggggagagtg atacagattc atttgaagaa gatcctgaaa   1200

tttccttagc tgactattgg aaatgcactt catgcaatga aatgaatccc cccttccat   1260

cacattgcaa cagatgttgg gcccttcgtg agaattggct tcctgaagat aaagggaaag   1320

ataaagggga aatctctgag aaagccaaac tggaaaactc aacacaagct gaagagggct   1380

ttgatgttcc tgattgtaaa aaaactatag tgaatgattc cagagagtca tgtgttgagg   1440

aaaatgatga taaaattaca caagcttcac aatcacaaga aagtgaagac tattctcagc   1500

catcaacttc tagtagcatt atttatagca gccaagaaga tgtgaaagag tttgaagggg   1560

aagaaaccca agacaaagaa gagagtgtgg aatctagttt gccccttaat gccattgaac   1620

cttgtgtgat ttgtcaaggt cgacctaaaa atggttgcat tgtccatggc aaaacaggac   1680

atcttatggc ctgctttaca tgtgcaaaga agctaaagaa aaggaataag ccctgcccag   1740

tatgtagaca accaattcaa atgattgtgc taacttattt cccctagttg acctgtctat   1800

aagagaatta tatatttcta actatataac cctaggaatt tagacaacct gaaatttatt   1860

cacatatatc aaagtgagaa aatgcctcaa ttcacataga tttcttctct ttagtataat   1920
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368

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tgacctactt tggtagtgga atagtgaata cttactataa tttgacttga atatgtagct    1980

catcctttac accaactcct aattttaaat aatttctact ctgtcttaaa tgagaagtac    2040

ttggtttttt ttttcttaaa tatgtatatg acatttaaat gtaacttatt attttttttg    2100

agaccgagtc ttgctctgtt acccaggctg gagtgcagtg ggtgatcttg gctcactgca    2160

agctctgccc tccccgggtt cgcaccattc tcctgcctca gcctcccaat tagcttggcc    2220

tacagtcatc tgccaccaca cctggctaat tttttgtact tttagtagag acagggtttc    2280

accgtgttag ccaggatggt ctcgatctcc tgacctcgtg atccgcccac ctcggcctcc    2340

caaagtgctg ggattacagg catgagccac cg                                  2372
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<210>  616
<211>  3198
<212>  DNA
<213>  Homo sapiens

<400>  616
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gtgccgctat gggagtcccg gcgttcttcc gctggctcag ccgcaagtac ccgtccatca     120

tagtcaactg cgtggaagag aagccaaaag aatgcaatgg tgtaaagatt ccagttgatg     180

ccagtaaacc taatccaaat gatgtggagt ttgataatct gtatttggat atgaatggaa     240

tcatccatcc ctgtactcat cctgaagaca aaccagcacc aaaaaatgaa gatgaaatga     300

tggttgcaat ttttgagtac attgacagac ttttcagtat tgtaagacca agaagacttc     360

tctacatggc aatagatgga gtggcaccac gtgtaaaaat gaaccagcag cgttcaagga     420

ggttcagggc catcaaaaga ggaatggaag cagcagtcga gaagcagcga gtcagggaag     480

aaatattggc aaaaggtggc tttcttcctc cagaagaaat aaaagaaaga tttgacagca     540

actgtattac accaggaact gaattcatgg acaatcttgc taaatgcctt cgctattaca     600

tagctgatcg tttaaataat gaccctgggt ggaaaaattt gacagttatt ttatctgatg     660

ctagtgctcc tggtgaagga aacataaaa tcatggatta cattagaagg caaagagccc     720

agcctaacca tgacccaaat actcatcatt gtttatgtgg agctgatgct gatctcatta     780

tgcttggcct tgccacacat gaaccgaact ttaccattat tagagaagaa ttcaaaccaa     840

acaggcccaa accatgtggt ctttgtaatc agtttggaca tgaggtcaaa gattgtgaag     900

gtttgtcaag agaaaagaag ggaaagcatg atgaacttgc cgatagtctt ccttgtgcag     960

aaggagagtt tatcttcctt cggcttaatg ttcttcgtga gtatttggaa agagaactca    1020

caatggccag cctaccattc acatttgatg ttgagaggag cattgatgac tgggtttttca    1080

tgtgcttctt tgtgggaaat gacttcctcc ctcatttgcc atcgttagag attagggaaa    1140
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369

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atgcaattga ccgtttggtt aacatataca aaaatgtggt acacaaaact ggggggttacc    1200

ttacagaaag tggttatgtc aatctgcaaa gagtacagat gatcatgtta gcagttggtg    1260

aagttgagga tagcattttt aaaaagagaa aggatgatga ggacagtttt agaagacgac    1320

agaaagaaaa aagaaagaga atgaagagag atcaaccagc tttcactcct agtggaatat    1380

taactcctca tgccttgggt tcaagaaatt caccaggttc tcaagtagcc agtaatccga    1440

gacaagcagc ctatgacatg aggatgcaga ataactctag tccttcgata tctcctaata    1500

cgagtttcac atctgatggc tccccgtctc cattaggagg aattaagcga aaagcagaag    1560

acagtgacag tgaacctgag ccagaggata atgtcaggtt atgggaagct ggctggaagc    1620

agcggtacta caagaacaaa tttgatgtgg atgcagctga tgagaaattc cgtcggaaag    1680

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tacgagctgc cctagaagag gtatacccag acctcactcc agaagagacc agaagaaaca    2100

gccttggagg tgatgtctta tttgtgggga aacatcaccc actccatgac ttcattttag    2160

agctgtacca gacaggttcc acagagccag tggaggtacc ccctgaacta tgtcatggga    2220

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cacagtttgc tgaagattac attttttaaag ctgtaatgct tccaggagca agaaagccag    2400

cagcagtact gaaacctagt gactggggaa aatccagcaa tggacggcag tggaagcctc    2460

agcttggctt taaccgtgac cggaggcctg tgcacctgga tcaggcagcc ttcaggactt    2520

tgggccatgt gatgccaaga ggctcaggaa ctggcattta cagcaatgct gcaccaccac    2580

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aacttatgtc aaatatgagg ccccaggatt cctggcgagg tcctcctccc cttttccagc    2700

agcaaaggtt tgacagaggc gttggggctg aacctctgct cccatggaac cggatgctgc    2760

aaacccagaa tgcagccttc cagccaaacc agtaccagat gctagctggg cctggtgggt    2820

atccacccag acgagatgat cgtggaggga cagggata tcccagagaa ggaaggaaat    2880

accctttgcc accacctca ggaagataca attggaatta agcttttgta aagctttccc    2940
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370

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aaatcctttc atcattctac agttttatgc tatttgtgga aagatttctt tctcaagtag      3000

tagttttaa  taaaactaca gtactttgtg tatttctttt aactgtgtat atttctactg      3060

atctgatctc actgtttatg ttgctttcca aagatgtatg ttgcataata cagtggatct      3120

gaatttatta atgcttataa acacatttga ggaataggag gtccgggttt tccataatgg      3180

gtaaaatgga accagctg                                                    3198
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<210>  617
<211>  422
<212>  DNA
<213>  Homo sapiens

<400>  617
tgagtgtaaa gaaaggttta ctccttgtat catcccctcc ccgtggactg cttcaattct        60

atcggggaca ggccagtccc tggaggctgc aaggagccac aaacctttcc cagctcacac       120

tctgcacccc tcagtctctg ctgctaaaga atcagactca ggtagatggg gtgtccacag       180

tctgtcctca ttacccagtc ataccgggta gcatggcccg agagagccct tatctctccc       240

caccttaaaa ccctcagcat cacacagcag gaaccagtcc acagggctta ccaaggatac       300

gcagtgaaaa cagaataatg tctgttacaa acccectaaa cctgagatgg ctgaagagcc       360

agattcctgc accccatctg actccccag  gcagtgggag atgacccaaa gcccccattc       420

cc                                                                      422
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<210>  618
<211>  287
<212>  DNA
<213>  Homo sapiens

<400>  618
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aatacaatgc aacaaaatat tcatatattg cacaaacagg gatgtgcata caaagatgct       120

aacaacattg gctggtaata ggctttacca tgttatgatc taaatgcttg ttcatcaaaa       180

aatgtacaaa attctaagtt tggcatccaa aaggggcttt acagttattg aatattttc        240

ccagccctat tttaaatcaa attcaagttt gcctatgaca aagactg                    287
```

```
<210>  619
<211>  515
<212>  DNA
<213>  Homo sapiens

<400>  619
tttttttttt tttttttttt tttttttttt tctgcttaat ggcatgagag ctccatgaag        60

gaatttatta gatacaccct gattctccac tgccctaaca cacgatactg agttgctaat       120
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gtccacattc agcaccaggg gaaattcgtg catcacatga catcgcctca ttaaagctgt   180

cagcataact ttaccaaaca agttatataa caaccaagaa gccactggta caggataata   240

ttcagaatgt gacatgtaaa aattgcaata agtagaatat attttttatg ttgttgaaca   300

aaagaaaatt gaaagaatta aagcaatcca agggcctaga agcaagtgaa ttctctgata   360

cctgtgagta aggctacttt aggacagccc atgaatccat tcctcgggtt gttctgagct   420

ccttgagaaa tggccccaac tgggtttttg gagtgaacct ggttcaatac agattgcctt   480

aggatgttca ctgaaagttt cggcttgctc tggac   515

<210>   620
<211>   1843
<212>   DNA
<213>   Homo sapiens

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ggaggaggtg gcggcgctgg agctcctccc ggggaccagc gacccgggga gcgagcacgt   60

cgctccgcac cgctcttcct ccagccgctg agccgtccct tctcgccatg tcccagagca   120

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agaccaagaa catcccagtt tatgaatgtg aaagatctga tgtgcaaata cacgtgccca   300

ctttcacctt cagagtaacc gttggtgaca taacctgcac aggtgaaggt acaagtaaga   360

agctggcgaa acatagagct gcagaggctg ccataaacat tttgaaagcc aatgcaagta   420

tttgctttgc agttcctgac cccttaatgc ctgacccttc caagcaacca aagaaccagc   480

ttaatcctat tggttcatta caggaattgg ctattcatca tggctggaga cttcctgaat   540

ataccctttc ccaggaggga ggacctgctc ataagagaga atatactaca atttgcaggc   600

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ttagtgaaat tgccaggaa caaggtttta atataacata tttggatata gatgaactga   900

gcgccaatgg acaatatcaa tgtcttgctg aactgtccac cagccccatc acagtctgtc   960

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cacataaaaa gttcccctct ggccccttcc caagtaaaac ttttaccgta gtgtttatgt   1140

cttgtttcta aatctcttca tagattccat caacactcca gatttaatta tctcctcata   1200

gttgttatta agctcttttt aatggcttca actttgtatc agtatactgt atttataaac   1260

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aactgcatgt ttgttgttga tgatgaaata aaaatgctag cgacagtctt tcttactggt   1380

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tagagtcttg agggacagca ctaacaggcc tttattaagt atgattgatt gttaaatttc   1500

agggaacatg attggtctgc tgtgtatttg aattcatgta acaaagaact gttacgatgg   1560

gattctgctc attttattaa aaagctactg acttgactgt catcctgttc ttgttagcca   1620

ttgtgaataa gattttaatg ttgataattc tgttatttac atatctctaa tttactttga   1680

aattcaaagg tgaaaataaa aaatgatggc ctaagtaaaa tttaaaaaaa aaaaaaaaaa   1740

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa   1800

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaccccc ggg   1843

<210> 621
<211> 267
<212> DNA
<213> Homo sapiens

<400> 621
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tccaatatac tgacccttgg gacttgggta ttgctggcct gctttgggcc ctcaggctct   120

ttgcctgctg gtttctgagc tttccatagt cacagtctgg ttttaggcag aaactgtacc   180

tccatttgca atcaacccctt ttgcagctgt gccttacgct tcttactgtg tttttaccaa   240

ttcatctgga acaaactaga aaaggaa   267

<210> 622
<211> 363
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (316)..(316)
<223> n is a, c, g, t or u

<400> 622
ctttgccatc aggtggtggt caacgaaggg gcccttcttc agcgaacgag tcatggccta   60

gcccttactt cttgcgacgc gagacgatga acgtctgcgt gcgcttgttg ttgcgagtgc   120

ggtagcccctt cgtcagggtg ttccacggcg acacagggac ctggccctcg ccggtgcggc   180

cttcgccacc accgtgcggg tgatccaccg ggttcatggc aacgccacga acggtcgggc   240

ggatgcccctt ccagcggatc gcgccggcct tgccgtactg gcgcaggctg tgctcttcgt   300

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tgctcacttc accganggtg gcgcggcagt cgatgtgcac gcggcggact tcgccggagc    360

gca                                                                  363
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<210>   623
<211>   345
<212>   DNA
<213>   Homo sapiens

<400>   623
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taagcacatc ccctcgaaat agcagcagct ctaaacatga aattcttcct ggaggatttt   120

cttactcttg agttctattc taccaaattt tttgagcact tactgtcagg cattcagaat   180

gtgagcaatg acaataattt acctacactt ttgcacttac agtatgctgg gcccagttga   240

ttctcaaaac agttctggga attagctata aaaatgcccc catcttacag atgaggaagc   300

tcaggctcag aaaggcaaaa aaaaaaaagc cctatagtga gtcgt                    345
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<210>   624
<211>   417
<212>   DNA
<213>   Homo sapiens

<400>   624
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ggaaaagwta cagaaaaama cctatcacam aggaaaagat aaatatgtyt gaytatytha   120

mmaggtgaaa cccataacca aaatttaaag gcaaattcac acaagtggaa atacagatgc   180

ccaactatcg tacaaagrga accatgwtca aggtcactaa caagcaaaga attttmagtt   240

tttbbtgttt ttbgttgttt ttyatttgrg acggrgtytc gytctgtcac ccaggctggr   300

gtscagtggc gcgatcttgg ytcactgcaa cctccgcctc ctgggttcaa gcaattctct   360

gcctcagcct cccaagtagc tgggdttaca ggcgcccgcc accacgcccg gctaatt      417
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<210>   625
<211>   2422
<212>   DNA
<213>   Homo sapiens

<400>   625
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<213>   Homo sapiens
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acctgaatgt gtctgcgtcc ctgttagcat aatgtgagga ggtggagaga cagcccaccc   1260

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<212> DNA
<213> Homo sapiens

<400> 631

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<400> 632

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tggctatctc ttcctggata tcatcactta tctggtattt gcagtcacct ttgtcctcgg   180

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gagaggcatc atccggttca tcattggctt cagcgcaccc atgtccatcg ttgctgtcag   720

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ctcccagctc cagcttcgtc tcaccttgag ttaggctgag cacaggcatt tcctgcttat    1200

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<213>  Homo sapiens

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ccatcgtgtg ggaagaacgg agtaacgagt ctcacgcaga aaaaggtctt gagagcacct     360

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aagaccagat tggaggctga tgaagtagct gcccagctag aacgctgtga caaagagaac    1920

aagatcctta aagatgagat gaacaaagag attgaggcgg cacgaaggca gttccagtct    1980

cagctggctg acctgcagca gctccctgac atcctgaaga tcacggaggc gaagctggct    2040

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agctgaaaaa tggcaaacaa aaagggcaag gcttttttta aaccccaaa aataaggttc     180

cacaaaaaag gacccgccaa aaccaaatta tagcggcaaa ttttttttgg ccataaatag    240

ggatcccctt aaaaatcctt ggaaactcct tggcagtttt aaggcccaaa ctaacccttg    300

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387

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acatcctctc gctcaggccg tcgtgcgcca cgtcgatgca accgatgtgc cgcgcttgcg       180

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ttcctactgg caccagagag agcaggacga cttcttcaaa ttcttgtgca aatacggcga       300

gaagaagtgc atgagaaagt gctttataag ctgtatagct ctcttgccta tgagagtatc       360

attgtagttc atctcacata accnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn       420

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<213>   Homo sapiens

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aataacagtc atttaacaca agacacaaat ttctttctgt ctcatgtaaa agaaacccaa       240

gcagcagtcc tgggccccca agtatcatca gtgactgtgg ctccttcttt ctttctgatc       300
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tgccatcctc caagtggggt ttccaccctc acagtcacct caagatgcaa gaacactgct    360

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tgagccttat cagtcaaaga ggaatgttaa tatgtaatag gaaatgaaga attggtgaaa    180

atactttgtg aaagaaacat aactttaaga tagtactata tctgaatccc ttgctgttcc    240

ctatatggtg ccttacacat cataagccag caaatacctt ggtctgattg aatggtaatg    300

ggatatattt tattaaaatc aaagttttgc tagggctggg aagctctacc aaaagaagaa    360

aaaattatct ttcttggtca tgtttccctc tttactccac gacagtttca ttattgtaac    420

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cagggggcac ccccacagtc acggtacccc acactgctac tcggctgagg aactgcccct    180

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cccctagact ggacacgtgt gctccccaga gggcacccccc tatttatgtg tatttattgt    720
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389

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taaccaaagc ttccttaact tgggaatctt gggaacctag aaagtgaggt aacccaagcc      180

aaattcctct ggtgtcacag ttcctcctat accaggccag gcacttgcca atgacactgg      240

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agaggtaatt ctttattctc gagagcttcc tcgtgcacat gatcagcttt tgcacatgct      360

tgaaggaaaa acaacactat taaaatgtct ttttaaaagt caaagctaaa tgagtatgca      420

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ggaatgagca ggacttaatt ctcatgccgg catggggctg ccgggcaccc agctcctttc      540

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attcagaaaa taaaggagta tcacagctct tttagaattt gtctagcagg ctttccagtt      5340

tttaccagaa aacccctata aattaaaaat tttttactta aatttaagaa ttaaaaaaat      5400

acaaaaaaga aaaatgaaa ataaaggaat aagaagttac ctactccaaa aaaaaaaa       5458
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<213> Homo sapiens

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cgcggtaatg ctggtggtct gcatcaccac cggatcaact tcgacaaata ccacccaggc      180

tacttgggga aagtgggtat gaagcattac cacttaaaga ggaaccagag cttctgccca      240

natgtcaacc ttgacaaatg tgtgggactt gggtcagtga acagacacgg gtgaatgctg      300

ctaaaaacaa gactggggct gctcccatca ttgatgtggt gcgatcgggc tactataaag      360

ttctgggaaa gggaaagctc ccaaagcagc ctgtcatcgt gaaggccaaa ttcttcagca      420

gaagagctga ggagaagatt acgagtgtgg gggggcctg tgtcctggtg gcttgaagcc      480

acatggaggg agttcataaa tggtatacca aaaaaaaga aaaaaaaaa attgtttggg      540

gcggggccca gaaaattcaa accacggtgc gggcgggcca gagatggcaa cgggccgagg      600

gcgcagagac cgggacgaca ggggggttcc acaaaaaagc gcgggccggg tgaagaacag      660

ggtccgccag ggtcgcaggc acggatcatc ccccgccgcg gcccacacac gacgacacag      720

acaaacgaag agacaagacc catctgatgt cctcagtctc aggcgacgac gtgccaggag      780

aggcgcgcag aaacactgca aaaaactgac accgcagcag gcccagccac ccacaaggca      840

aaagtgccac cgacgcgcgc aaccggagcg ccaaagccga ccaagacga gaagaaccga      900

cacgagcagc acaagggcgg cgacgcggaa ggagacagga gccacggcag acggaccaga      960
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cacgatgcaa cacacgcaaa gacgcaccca agacagaacg gacagacaca aacaaggaga    1020

aagcaggaga actaccgacc gcgacgcaag agacacagaa aacagagggg aacgaggcag    1080

agaaaagaga acgagcgcga acgcgacgga tcaaggcgag cagaccagac acagaacagc    1140

ggggacacag cagaagaacg aagaacaaca gagacgcgac agaaagacaa agaaccgcag    1200

agcagacacc aggccaagag caagagggga gaacacacag cgagggaacg agcgagagag    1260

agatgagaaa tacagacatg aaggaagacg agcaaggaca cagcgagagt ccaggaacag    1320

gcagacaagc gagaaagagg agaagcgcaa cacgaacaga aaaccagagc gag           1373
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<213>    Homo sapiens

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ccaccagctg cctccttctc ttggccctct tggtacaggg aggagcagct gcgcccatca    180

gctcccactg caggcttgac aagtccaact tccagcagcc ctatatcacc aaccgcacct    240

tcatgctggc taaggaggct agcttggctg ataacaacac agacgttcgt ctcattgggg    300

agaaactgtt ccacggagtc agtatgagtg agcgctgcta tctgatgaag caggtgctga    360

acttcaccct tgaagaagtg ctgttccctc aatctgatag gttccagcct tatatgcagg    420

aggtggtgcc cttcctggcc aggctcagca acaggctaag cacatgtcat attgaaggtg    480

atgacctgca tatccagagg aatgtgcaaa agctgaagga cacagtgaaa aagcttggag    540

agagtggaga gatcaaagca attggagaac tggatttgct gtttatgtct ctgagaaatg    600

cctgcatttg accagagcaa agctgaaaaa tgaataacta accccctttc cctgctagaa    660

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<211>    1189
<212>    DNA
<213>    Homo sapiens

<400>    661
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ataaagttca gaaacatgt ctcgaagata tgactccagg accactatat tttctccaga    180

aggtcgctta taccaagttg aatatgccat ggaagctatt ggacatgcag gcacctgttt    240
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gggaatttta gcaaatgatg gtgttttgct tgcagcagag agacgcaaca tccacaagct      300

tcttgatgaa gtcttttttt ctgaaaaaat ttataaactc aatgaggaca tggcttgcag      360

tgtggcaggc ataacttctg atgctaatgt tctgactaat gaactaaggc tcattgctca      420

aaggtattta ttacagtatc aggagccaat accttgtgag cagttggtta cagcgctgtg      480

tgatatcaaa caagcttata cacaatttgg aggaaaacgt ccctttggtg tttcattgct      540

gtacattggc tgggataagc actatggctt tcagctctat cagagtgacc ctagtggaaa      600

ttacggggga tggaaggcca catgcattgg aaataatagc gctgcagctg tgtcaatgtt      660

gaaacaagac tataagaag gagaaatgac cttgaagtca gcacttgctt tagctatcaa      720

agtactaaat aagaccatgg atgttagtaa actctctgct gaaaaagtgg aaattgcaac      780

actaacaaga gagaatggaa agacagtaat cagagttctc aaacaaaaag aagtggagca      840

gttgatcaaa aaacatgagg aagaagaagc caaagctgag cgtgagaaga agaaaaaga      900

acagaaagaa aaggataaat agaatcagag attttattac tcatttgggg caccatttca      960

gtgtaaaagc agtcctactc ttccacacta ggaaggcttt actttttta actggtgcag     1020

tgggaaaata ggacattaca tactgaattg ggtccttgtc atttctgtcc aattgaatac     1080

tttattgtaa cgatgatggt tacccttcat ggacgtctta atcttccaca cacatcccct     1140

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gccgggggtc atcatggaac taattcgctg accgacccag cggccgcagc cgtgcgtccc      300

gctcgagcgc cagcgcccgc gcccgcgccc cccgatccgc ttccccttc tccctcctca      360

gttggccgag tcgtcccgcg cgcaccgcct ccgcgcgcct atgagaatga ggtggtaacg      420

ggcccccgga tgaccccgcg tcaccactgt gaggcctaca gctctgccgg ggaggaggag      480

gaggaggaag aggaggagaa ggtagctaca gcaagctggg tagcaggcag atccaaagga      540

tatcatgaag tttccagggc ctttggaaaa ccagagattg tctttcctgt tggaaaaggc      600

aatcactagg gaagcacaga tgtggaaagt gaatgtgcgg aaaatgcctt caaatcagaa      660
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tgtttctcca tcccagagag atgaagtaat tcaatggctg gccaaactca agtaccaatt       720

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caagactgtt gaggaagatg agagaattcc agtactaaag gtattggcaa gagacagttt       900

ctgtggatgt tcctcatctg aaattttgag aatggagaga attattctgg ataagttgaa       960

ttgggatctt cacacagcca caccattgga ttttcttcat attttccatg ccattgcagt      1020

gtcaactagg cctcagttac ttttcagttt gcccaaattg agcccatctc aacatttggc      1080

agtccttacc aagcaactac ttcactgtat ggcctgcaac caacttctgc aattcagagg      1140

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ctctactaaa cgcaaagtag aggaaatgga agtggatgac ttctatgatg gaatcaaacg      1560

gctctataat gaagataatg tctcagaaaa tgtgggttct gtgtgtggca ctgatttatc      1620

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tcaacaagtg ctacctttga gtgtaaacta aggtagacta ctttgggaat gagaacatgc      1740

aaaatcagga aaggctgtag aaggaaatat accttaacag gctgatttgg agtgagccag      1800

aaaaaaaaaa taaaactctc attatttgtg tggctaatta taattcagcg ttatttaagc      1860

acataaagac caaaaaaaaa aaaaaaaaa                                        1890
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<212> DNA
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<400> 663
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accaagagat gaaagagggc tgcacgcgtg ggggcccgag tggtgggcgg ggacagtcgt       120

cttgttacag gggtgctggc cttccctggc gcctgcccct gtcggccccg cccgagaacc       180

tccctgcgcc agggcagggt ttactcatcc cggcgaggtg atcccatgcg cgagggcggg       240

cgcaagggcg gccagagaac ccagcaatcc gagtatgcgg catcagccct tcccaccagg       300

cacttccttc cttttcccga acgtccaggg agggagggcc gggcacttat aaactcgagc       360
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cctggccgat ccgcatgtca gaggctgcct cgcaggggct gcgcgcacgg caagaagtgt    420

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taccttcgag tgcatctgcg ggcccgactc ggcccttgcc cgccacattg gcaccgactg   1980

tgactccggc aaggtggacg gtggcgacag cggctctggc gagcccccgc ccagcccgac   2040

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atagttattt atttattgga gataatctag aacacaggca aaatccttgc ttatgacatc   4020
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419

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cagaagcatg tttattgctt cagaataagc actccccaag cattagaaga tgctctgtat   420

agtgaatatc tctatcagga acagtatttt attaaaaagg atagcaaaga agaaatatat   480

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ccattggtag cgctattgac cttagctgat gaggatgacc gggaaattta tgatattatt   600

tccatggtgt cagtgattca tattcctgat aggacttata aactatcctg cagaatattg   660

tatcaatatt tactcttggc tcaaggtcaa tttcatgatc ttaagcaact tttcatgtct   720

gcaaataata atttcactcc ctccaacaat tcctcttcag aagaaaaaaa cacagacaga   780

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acatgcctgt gtgatggctg tgtgaagtat tttcagcagt gcccaatgtg caggcagttt   960

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tcttggaatt catcataaca tggaatctac agtactgacc atcaatgaaa attatatttt   1140

aacttcatat ttgtatggta cttggatgat aaaaattaat tattcctttc tgcttagtga   1200

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<212> DNA
<213> Homo sapiens

<400> 665
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tgacgcattc taatcatgtg gcgatcttg                                   29


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cccctaaaa tcccactgta aacaaacatt tcg                               33


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agctgcaact ttacagggac ttgaaaagaa agaaaa                           36


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gggaagacag acagcagcag accca   25

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tgccacttct ggtctcgtcg gtga   24

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<400> 2390
accaacttac tcttaaaaag gatggctgcc aaga   34

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<400> 2391
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cccaaagaag ggtcagccaa agcca   25

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ggcctggtgt ctgctctgcg g   21

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1   5   10   15

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     Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
              35                  40                  45

     Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile
              50                  55                  60

     Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
     65                  70                  75                  80

     Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
                      85                  90                  95

     Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
                      100                 105                 110

     Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
                      115                 120                 125

     Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
              130                 135                 140

     Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
     145                 150                 155                 160

     His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
                      165                 170                 175

     Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met Lys Ile
                      180                 185                 190

     Leu Thr Glu Arg Gly Tyr Ser Phe Thr Thr Thr Ala Glu Arg Glu Ile
              195                 200                 205

     Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp Phe Glu
              210                 215                 220

     Gln Glu Met Ala Thr Ala Ala Ser Ser Ser Leu Glu Lys Ser Tyr
     225                 230                 235                 240

     Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg Phe Arg
                      245                 250                 255
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677

Cys Pro Glu Ala Leu Phe Gln Pro Ser Phe Leu Gly Met Glu Ser Cys
              260   265   270

Gly Ile His Glu Thr Thr Phe Asn Ser Ile Met Lys Cys Asp Val Asp
              275   280   285

Ile Arg Lys Asp Leu Tyr Ala Asn Thr Val Leu Ser Gly Gly Thr Thr
              290   295   300

Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr Ala Leu
    305   310   315   320

Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu Arg Lys
                  325   330   335

Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser Thr Phe
                  340   345   350

Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ser Gly Pro Ser
        355   360   365

Ile Val His Arg Lys Cys Phe
    370   375

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<400> 2401

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Trp Gly Cys Ala Leu Gly Leu Gln Gly Gly Met Leu Tyr Pro Gln Glu
              20   25   30

Ser Pro Ser Arg Glu Cys Lys Glu Leu Asp Gly Leu Trp Ser Phe Arg
        35   40   45

Ala Asp Phe Ser Asp Asn Arg Arg Arg Gly Phe Glu Glu Gln Trp Tyr
    50   55   60

Arg Arg Pro Leu Trp Glu Ser Gly Pro Thr Val Asp Met Pro Val Pro
65   70   75   80

Ser Ser Phe Asn Asp Ile Ser Gln Asp Trp Arg Leu Arg His Phe Val
              85   90   95

678

Gly Trp Val Trp Tyr Glu Arg Glu Val Ile Leu Pro Glu Arg Trp Thr
        100   105   110

Gln Asp Leu Arg Thr Arg Val Val Leu Arg Ile Gly Ser Ala His Ser
        115   120   125

Tyr Ala Ile Val Trp Val Asn Gly Val Asp Thr Leu Glu His Glu Gly
    130   135   140

Gly Tyr Leu Pro Phe Glu Ala Asp Ile Ser Asn Leu Val Gln Val Gly
145   150   155   160

Pro Leu Pro Ser Arg Leu Arg Ile Thr Ile Ala Ile Asn Asn Thr Leu
            165   170.   175

Thr Pro Thr Thr Leu Pro Pro Gly Thr Ile Gln Tyr Leu Thr Asp Thr
        180   185   190

Ser Lys Tyr Pro Lys Gly Tyr Phe Val Gln Asn Thr Tyr Phe Asp Phe
        195   200   205

Phe Asn Tyr Ala Gly Leu Gln Arg Ser Val Leu Leu Tyr Thr Thr Pro
    210   215   220

Thr Thr Tyr Ile Asp Asp Ile Thr Val Thr Thr Ser Val Glu Gln Asp
225   230   235   240

Ser Gly Leu Val Asn Tyr Gln Ile Ser Val Lys Gly Ser Asn Leu Phe
            245   250   255

Lys Leu Glu Val Arg Leu Leu Asp Ala Glu Asn Lys Val Val Ala Asn
            260   265   270

Gly Thr Gly Thr Gln Gly Gln Leu Lys Val Pro Gly Val Ser Leu Trp
    275   280   285

Trp Pro Tyr Leu Met His Glu Arg Pro Ala Tyr Leu Tyr Ser Leu Glu
    290   295   300

Val Gln Leu Thr Ala Gln Thr Ser Leu Gly Pro Val Ser Asp Phe Tyr
305   310   315   320

Thr Leu Pro Val Gly Ile Arg Thr Val Ala Val Thr Lys Ser Gln Phe
            325   330   335

679

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Leu Ile Asn Gly Lys Pro Phe Tyr Phe His Gly Val Asn Lys His Glu
            340             345             350

Asp Ala Asp Ile Arg Gly Lys Gly Phe Asp Trp Pro Leu Leu Val Lys
            355             360             365

Asp Phe Asn Leu Leu Arg Trp Leu Gly Ala Asn Ala Phe Arg Thr Ser
    370             375      .      380

His Tyr Pro Tyr Ala Glu Glu Val Met Gln Met Cys Asp Arg Tyr Gly
385             390             395             400

Ile Val Val Ile Asp Glu Cys Pro Gly Val Gly Leu Ala Leu Pro Gln
            405             410             415

Phe Phe Asn Asn Val Ser Leu His His His Met Gln Val Met Glu Glu
            420             425             430

Val Val Arg Arg Asp Lys Asn His Pro Ala Val Val Met Trp Ser Val
            435             440             445              .

Ala Asn Glu Pro Ala Ser His Leu Glu Ser Ala Gly Tyr Tyr Leu Lys
    450             455             460

Met Val Ile Ala His Thr Lys Ser Leu Asp Pro Ser Arg Pro Val Thr
465             470             475             480

Phe Val Ser Asn Ser Asn Tyr Ala Ala Asp Lys Gly Ala Pro Tyr Val
            485             490             495

Asp Val Ile Cys Leu Asn Ser Tyr Tyr Ser Trp Tyr His Asp Tyr Gly
            500             505             510

His Leu Glu Leu Ile Gln Leu Gln Leu Ala Thr Gln Phe Glu Asn Trp
            515             520             525

Tyr Lys Lys Tyr Gln Lys Pro Ile Ile Gln Ser Glu Tyr Gly Ala Glu
    530             535             540

Thr Ile Ala Gly Phe His Gln Asp Pro Pro Leu Met Phe Thr Glu Glu
545             550             555             560

Tyr Gln Lys Ser Leu Leu Glu Gln Tyr His Leu Gly Leu Asp Gln Lys
            565             570             575
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Arg Arg Lys Tyr Val Val Gly Glu Leu Ile Trp Asn Phe Ala Asp Phe
            580             585             590


Met Thr Glu Gln Ser Pro Thr Arg Val Leu Gly Asn Lys Lys Gly Ile
            595             600             605


Phe Thr Arg Gln Arg Gln Pro Lys Ser Ala Ala Phe Leu Leu Arg Glu
    610             615             620


Arg Tyr Trp Lys Ile Ala Asn Glu Thr Arg Tyr Pro His Ser Val Ala
625             630             635             640


Lys Ser Gln Cys Leu Glu Asn Ser Pro Phe Thr
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<400> 2402

```
Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1               5               10              15


Gly Leu Glu Ala Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg
            20              25              30


His Pro Ala Glu Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser
            35              40              45


Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu
    50              55              60


Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp
65              70              75              80


Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp
            85              90              95


Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile
            100             105             110


Val Lys Trp Asp Arg Asp Met
            115
```

<210> 2403
<211> 228

<212> PRT
<213> Homo sapiens

<400> .2403

```
Met Ser Val Ser Glu Ile Phe Val Glu Leu Gln Gly Phe Leu Ala Ala
1               5                  10                 15

Glu Gln Asp Ile Arg Glu Glu Ile Arg Lys Val Val Gln Ser Leu Glu
                20                 25                 30

Gln Thr Ala Arg Glu Ile Leu Thr Leu Leu Gln Gly Val His Gln Gly
        35                 40                 45

Ala Gly Phe Gln Asp Ile Pro Lys Arg Cys Leu Lys Ala Arg Glu His
        50                 55                 60

Phe Gly Thr Val Lys Thr His Leu Thr Ser Leu Lys Thr Lys Phe Pro
65                 70                 75                 80

Ala Glu Gln Tyr Tyr Arg Phe His Glu His Trp Arg Phe Val Leu Gln
                85                 90                 95

Arg Leu Val Phe Leu Ala Ala Phe Val Val Tyr Leu Glu Thr Glu Thr
                100                105                110

Leu Val Thr Arg Glu Ala Val Thr Glu Ile Leu Gly Ile Glu Pro Asp
        115                120                125

Arg Glu Lys Gly Phe His Leu Asp Val Glu Asp Tyr Leu Ser Gly Val
        130                135                140

Leu Ile Leu Ala Ser Glu Leu Ser Arg Leu Ser Val Asn Ser Val Thr
145                150                155                160

Ala Gly Asp Tyr Ser Arg Pro Leu His Ile Ser Thr Phe Ile Asn Glu
                165                170                175

Leu Asp Ser Gly Phe Arg Leu Leu Asn Leu Lys Asn Asp Ser Leu Arg
                180                185                190

Lys Arg Tyr Asp Gly Leu Lys Tyr Asp Val Lys Lys Val Glu Glu Val
        195                200                205

Val Tyr Asp Leu Ser Ile Arg Gly Phe Asn Lys Glu Thr Ala Ala Ala
210                215                220
```

Cys Val Glu Lys
225

<210> 2404
<211> 378
<212> PRT
<213> Homo sapiens

<400> 2404

Met Asp Leu Gly Lys Pro Met Lys Ser Val Leu Val Val Ala Leu Leu
1   5   10   15

Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp Tyr
            20   25   30

Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu Cys
        35   40   45

Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp Phe Leu Pro Ile Met
    50   55   60

Tyr Ser Ile Ile Cys Phe Val Gly Leu Leu Gly Asn Gly Leu Val Val
65   70   75   80

Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr Tyr
                85   90   95

Leu Leu Asn Leu Ala Val Ala Asp Ile Leu Phe Leu Leu Thr Leu Pro
            100   105   110

Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His Phe
        115   120   125

Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly Met
    130   135   140

Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val Gln
145   150   155   160

Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser Lys
                165   170   175

Leu Ser Cys Val Gly Ile Trp Ile Leu Ala Thr Val Leu Ser Ile Pro
                180   185   190

Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala Met
            195   200   205

683

Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile Gln
    210   215   220

Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met Ser
225   230   235   240

Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn Phe
            245   250   255

Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val Phe
            260   265   270

Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr Val
        275   280   285

Ala Asn Phe Asn Ile Thr Ser Ser Thr Cys Glu Leu Ser Lys Gln Leu
    290   295   300

Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys Cys
305   310   315   320

Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn Asp
            325   330   335

Leu Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln Leu
            340   345   350

Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser Val
        355   360   365

Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro
    370   375

<210> 2405
<211> 398
<212> PRT
<213> Homo sapiens

<400> 2405

Met Leu Arg Leu Tyr Val Leu Val Met Gly Val Ser Ala Phe Thr Leu
1   5   10   15

Gln Pro Ala Ala His Thr Gly Ala Ala Arg Ser Cys Arg Phe Arg Gly
        20   25   30

```
Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
        35              40              45

Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
        50              55              60

Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
65              70              75              80

Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
                85              90              95

Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
            100             105             110

Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
        115             120             125

Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
    130             135             140

Ser Thr Ser Gly Val Leu Val Cys Pro Asp Leu Ser Glu Phe Thr Arg
145             150             155             160

Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
            165             170             175

Asp Lys Asp Asn Glu Lys Phe Leu Ser Val Arg Gly Thr Thr His Leu
        180             185             190

Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
    195             200             205

Leu Thr Phe Ala His Glu Gly Gln Gln Tyr Asn Ile Thr Arg Ser Ile
    210             215             220

Glu Leu Arg Ile Lys Lys Lys Glu Glu Thr Ile Pro Val Ile Ile
225             230             235             240

Ser Pro Leu Lys Thr Ile Ser Ala Ser Leu Gly Ser Arg Leu Thr Ile
            245             250             255

Pro Cys Lys Val Phe Leu Gly Thr Gly Thr Pro Leu Thr Thr Met Leu
        260             265             270

Trp Trp Thr Ala Asn Asp Thr His Ile Glu Ser Ala Tyr Pro Gly Gly
```

```
                 275                        280                         285
```

Arg Val Thr Glu Gly Pro Arg Gln Glu Tyr Ser Glu Asn Asn Glu Asn
        290   295   300

Tyr Ile Glu Val Pro Leu Ile Phe Asp Pro Val Thr Arg Glu Asp Leu
305   310   315   320

His Met Asp Phe Lys Cys Val Val His Asn Thr Leu Ser Phe Gln Thr
            325   330   335

Leu Arg Thr Thr Val Lys Glu Ala Ser Ser Thr Phe Ser Trp Gly Ile
        340   345   350

Val Leu Ala Pro Leu Ser Leu Ala Phe Leu Val Leu Gly Gly Ile Trp
        355   360   365

Met His Arg Arg Cys Lys His Arg Thr Gly Lys Ala Asp Gly Leu Thr
    370   375   380

Val Leu Trp Pro His His Gln Asp Phe Gln Ser Tyr Pro Lys
385   390   395

```
<210>   2406
<211>   132
<212>   PRT
<213>   Homo sapiens

<400>   2406
```

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1   5   10   15

Ile Cys Gly Gly Arg Val Val Cys Arg Pro Lys Lys Thr Glu Val Ser
            20   25   30

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
            35   40   45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
    50   55   60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65   70   75   80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
            85   90   95

Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
            100   105   110

Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
            115   120   125

Ile Leu Lys Met
        130

<210>   2407
<211>   587
<212>   PRT
<213>   Homo sapiens

<400>   2407

Met Val Thr Ala Ala Met Leu Leu Gln Cys Cys Pro Val Leu Ala Arg
1   5   10   15

Gly Pro Thr Ser Leu Leu Gly Lys Val Val Lys Thr His Gln Phe Leu
            20   25   30

Phe Gly Ile Gly Arg Cys Pro Ile Leu Ala Thr Gln Gly Pro Asn Cys
            35   40   45

Ser Gln Ile His Leu Lys Ala Thr Lys Ala Gly Gly Asp Ser Pro Ser
        50   55   60

Trp Ala Lys Gly His Cys Pro Phe Met Leu Ser Glu Leu Gln Asp Gly
65   70   75   80

Lys Ser Lys Ile Val Gln Lys Ala Ala Pro Glu Val Gln Glu Asp Val
                85   90   95

Lys Ala Phe Lys Thr Asp Leu Pro Ser Ser Leu Val Ser Val Ser Leu
            100   105   110

Arg Lys Pro Phe Ser Gly Pro Gln Glu Gln Glu Gln Ile Ser Gly Lys
            115   120   125

Val Thr His Leu Ile Gln Asn Asn Met Pro Gly Asn Tyr Val Phe Ser
        130   135   140

Tyr Asp Gln Phe Phe Arg Asp Lys Ile Met Glu Lys Lys Gln Asp His
145   150   155   160

Thr Tyr Arg Val Phe Lys Thr Val Asn Arg Trp Ala Asp Ala Tyr Pro

                    165   170   175

Phe Ala Gln His Phe Phe Glu Ala Ser Val Ala Ser Lys Asp Val Ser
            180   185   190

Val Trp Cys Ser Asn Asp Tyr Leu Gly Met Ser Arg His Pro Gln Val
        195   200   205

Leu Gln Ala Thr Gln Glu Thr Leu Gln Arg His Gly Ala Gly Ala Gly
        210   215   220

Gly Thr Arg Asn Ile Ser Gly Thr Ser Lys Phe His Val Glu Leu Glu
225   230   235   240

Gln Glu Leu Ala Glu Leu His Gln Lys Asp Ser Ala Leu Leu Phe Ser
            245   250   255

Ser Cys Phe Val Ala Asn Asp Ser Thr Leu Phe Thr Leu Ala Lys Ile
            260   265   270

Leu Pro Gly Cys Glu Ile Tyr Ser Asp Ala Gly Asn His Ala Ser Met
            275   280   285

Ile Gln Gly Ile Arg Asn Ser Gly Ala Ala Lys Phe Val Phe Arg His
        290   295   300

Asn Asp Pro Asp His Leu Lys Lys Leu Leu Glu Lys Ser Asn Pro Lys
305   310   315   320

Ile Pro Lys Ile Val Ala Phe Glu Thr Val His Ser Met Asp Gly Ala
            325   330   335

Ile Cys Pro Leu Glu Glu Leu Cys Asp Val Ser His Gln Tyr Gly Ala
            340   345   350

Leu Thr Phe Val Asp Glu Val His Ala Val Gly Leu Tyr Gly Ser Arg
            355   360   365

Gly Ala Gly Ile Gly Glu Arg Asp Gly Ile Met His Lys Ile Asp Ile
370   375   380

Ile Ser Gly Thr Leu Gly Lys Ala Phe Gly Cys Val Gly Gly Tyr Ile
385   390   395   400

Ala Ser Thr Arg Asp Leu Val Asp Met Val Arg Ser Tyr Ala Ala Gly
            405   410   415

```
Phe Ile Phe Thr Thr Ser Leu Pro Pro Met Val Leu Ser Gly Ala Leu
            420             425             430

Glu Ser Val Arg Leu Leu Lys Gly Glu Glu Gly Gln Ala Leu Arg Arg
            435             440             445

Ala His Gln Arg Asn Val Lys His Met Arg Gln Leu Leu Met Asp Arg
    450             455             460

Gly Leu Pro Val Ile Pro Cys Pro Ser His Ile Ile Pro Ile Arg Val
465             470             475             480

Gly Asn Ala Ala Leu Asn Ser Lys Leu Cys Asp Leu Leu Leu Ser Lys
            485             490             495

His Gly Ile Tyr Val Gln Ala Ile Asn Tyr Pro Thr Val Pro Arg Gly
            500             505             510

Glu Glu Leu Leu Arg Leu Ala Pro Ser Pro His His Ser Pro Gln Met
            515             520             525

Met Glu Asp Phe Val Glu Lys Leu Leu Leu Ala Trp Thr Ala Val Gly
    530             535             540

Leu Pro Leu Gln Asp Val Ser Val Ala Ala Cys Asn Phe Cys Arg Arg
545             550             555             560

Pro Val His Phe Glu Leu Met Ser Glu Trp Glu Arg Ser Tyr Phe Gly
            565             570             575

Asn Met Gly Pro Gln Tyr Val Thr Thr Tyr Ala
            580             585
```

```
<210>   2408
<211>   122
<212>   PRT
<213>   Homo sapiens

<400>   2408
```

```
Met Ser Ala Thr Trp Cys Ser Pro Glu Gly Gln Gly Met Gly Gln Gly
1               5               10              15

Pro Gly Arg Glu Val Gly Gly Asn Ser Ala Ala Ser Gly Pro Ala Ser
            20              25              30
```

```
Pro Ile Arg Asp Pro Cys Leu Ser Glu Ala Gly Leu Lys Gly Pro Pro
        35                  40                  45


Ser Ala His Pro Arg Arg Leu Cys Leu Leu His Arg Leu Val Cys Phe
    50                  55                  60


Ser Gly Gly Leu Thr Ser Ile Gln Leu Ser Pro Arg Thr Cys Cys Ser
65                  70                  75                  80


His Gln Trp Ala Gln Leu Phe Ser Pro Ala Cys Phe Pro Gln Trp Arg
                85                  90                  95


Ala Pro Gly Cys Ser Leu Asp Asp Ser Arg Ser Leu Thr Arg Ile Arg
            100                 105                 110


Pro Val His Leu Pro Gly Pro Ser Leu Asp
        115                 120


<210>   2409
<211>   288
<212>   PRT
<213>   Homo sapiens

<400>   2409

Met Gly His Thr Arg Arg Gln Gly Thr Ser Pro Ser Lys Cys Pro Tyr
1               5                   10                  15


Leu Asn Phe Phe Gln Leu Leu Val Leu Ala Gly Leu Ser His Phe Cys
            20                  25                  30


Ser Gly Val Ile His Val Thr Lys Glu Val Lys Glu Val Ala Thr Leu
        35                  40                  45


Ser Cys Gly His Asn Val Ser Val Glu Glu Leu Ala Gln Thr Arg Ile
    50                  55                  60


Tyr Trp Gln Lys Glu Lys Lys Met Val Leu Thr Met Met Ser Gly Asp
65                  70                  75                  80


Met Asn Ile Trp Pro Glu Tyr Lys Asn Arg Thr Ile Phe Asp Ile Thr
                85                  90                  95


Asn Asn Leu Ser Ile Val Ile Leu Ala Leu Arg Pro Ser Asp Glu Gly
            100                 105                 110


Thr Tyr Glu Cys Val Val Leu Lys Tyr Glu Lys Asp Ala Phe Lys Arg
        115                 120                 125
```

```
Glu His Leu Ala Glu Val Thr Leu Ser Val Lys Ala Asp Phe Pro Thr
    130                 135                 140

Pro Ser Ile Ser Asp Phe Glu Ile Pro Thr Ser Asn Ile Arg Arg Ile
145                 150                 155                 160

Ile Cys Ser Thr Ser Gly Gly Phe Pro Glu Pro His Leu Ser Trp Leu
                165                 170                 175

Glu Asn Gly Glu Glu Leu Asn Ala Ile Asn Thr Thr Val Ser Gln Asp
            180                 185                 190

Pro Glu Thr Glu Leu Tyr Ala Val Ser Ser Lys Leu Asp Phe Asn Met
        195                 200                 205

Thr Thr Asn His Ser Phe Met Cys Leu Ile Lys Tyr Gly His Leu Arg
    210                 215                 220

Val Asn Gln Thr Phe Asn Trp Asn Thr Thr Lys Gln Glu His Phe Pro
225                 230                 235                 240

Asp Asn Leu Leu Pro Ser Trp Ala Ile Thr Leu Ile Ser Val Asn Gly
            245                 250                 255

Ile Phe Val Ile Cys Cys Leu Thr Tyr Cys Phe Ala Pro Arg Cys Arg
            260                 265                 270

Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val Arg Pro Val
        275                 280                 285
```

```
<210>   2410
<211>   588
<212>   PRT
<213>   Homo sapiens

<400>   2410
```

```
Met His Cys Lys Val Ser Leu Leu Asp Asp Thr Val Tyr Glu Cys Val
1                   5                   10                  15

Val Glu Lys His Ala Lys Gly Gln Asp Leu Leu Lys Arg Val Cys Glu
            20                  25                  30

His Leu Asn Leu Leu Glu Glu Asp Tyr Phe Gly Leu Ala Ile Trp Asp
    35                  40                  45
```

Asn Ala Thr Ser Lys Thr Trp Leu Asp Ser Ala Lys Glu Ile Lys Lys
    50   55   60

Gln Val Arg Gly Val Pro Trp Asn Phe Thr Phe Asn Val Lys Phe Tyr
65   70   75   80

Pro Pro Asp Pro Ala Gln Leu Thr Glu Asp Ile Thr Arg Tyr Tyr Leu
                85   90   95

Cys Leu Gln Leu Arg Gln Asp Ile Val Ala Gly Arg Leu Pro Cys Ser
            100   105   110

Phe Ala Thr Leu Ala Leu Leu Gly Ser Tyr Thr Ile Gln Ser Glu Leu
            115   120   125

Gly Asp Tyr Asp Pro Glu Leu His Gly Val Asp Tyr Val Ser Asp Phe
    130   135   140

Lys Leu Ala Pro Asn Gln Thr Lys Glu Leu Glu Glu Lys Val Met Glu
145   150   155   160

Leu His Lys Ser Tyr Arg Ser Met Thr Pro Ala Gln Ala Asp Leu Glu
            165   170   175

Phe Leu Glu Asn Ala Lys Lys Leu Ser Met Tyr Gly Val Asp Leu His
            180   185   190

Lys Ala Lys Asp Leu Glu Gly Val Asp Ile Ile Leu Gly Val Cys Ser
            195   200   205

Ser Gly Leu Leu Val Tyr Lys Asp Lys Leu Arg Ile Asn Arg Phe Pro
    210   215   220

Trp Pro Lys Val Leu Lys Ile Ser Tyr Lys Arg Ser Ser Phe Phe Ile
225   230   235   240

Lys Ile Arg Pro Gly Glu Gln Glu Gln Tyr Glu Ser Thr Ile Gly Phe
                245   250   255

Lys Leu Pro Ser Tyr Arg Ala Ala Lys Lys Leu Trp Lys Val Cys Val
            260   265   270

Glu His His Thr Phe Phe Arg Leu Thr Ser Thr Asp Thr Ile Pro Lys
            275   280   285

Ser Lys Phe Leu Ala Leu Gly Ser Lys Phe Arg Tyr Ser Gly Arg Thr

Gln Ala Gln Thr Arg Gln Ala Ser Ala Leu Ile Asp Arg Pro Ala Pro
305   310   315   320

His Phe Glu Arg Thr Ala Ser Lys Arg Ala Ser Arg Ser Leu Asp Gly
              325   330   335

Ala Ala Ala Val Asp Ser Ala Asp Arg Ser Pro Arg Pro Thr Ser Ala
          340   345   350

Pro Ala Ile Thr Gln Gly Gln Val Ala Glu Gly Gly Val Leu Asp Ala
      355   360   365

Ser Ala Lys Lys Thr Val Val Pro Lys Ala Gln Lys Glu Thr Val Lys
  370   375   380

Ala Glu Val Lys Lys Glu Asp Glu Pro Pro Glu Gln Ala Glu Pro Glu
385   390   395   400

Pro Thr Glu Ala Trp Lys Lys Lys Arg Glu Arg Leu Asp Gly Glu Asn
              405   410   415

Ile Tyr Ile Arg His Ser Asn Leu Met Leu Glu Asp Leu Asp Lys Ser
          420   425   430

Gln Glu Glu Ile Lys Lys His His Ala Ser Ile Ser Glu Leu Lys Lys
      435   440   445

Asn Phe Met Glu Ser Val Pro Glu Pro Arg Pro Ser Glu Trp Asp Lys
  450   455   460

Arg Leu Ser Thr His Ser Pro Phe Arg Thr Leu Asn Ile Asn Gly Gln
465   470   475   480

Ile Pro Thr Gly Glu Gly Pro Pro Leu Val Lys Thr Gln Thr Val Thr
              485   490   495

Ile Ser Asp_Asn Ala Asn Ala Val Lys Ser Glu Ile Pro Thr Lys Asp
              500   505   510

Val Pro Ile Val His Thr Glu Thr Lys Thr Ile Thr Tyr Glu Ala Ala
      515   520   525

Gln Thr Val Lys Gly Gly Ile Ser Glu Thr Arg Ile Glu Lys Arg Ile
  530   535   540

```
Val Ile Thr Gly Asp Ala Asp Ile Asp His Asp Gln Val Leu Val Gln
545             550             555             560


Ala Ile Lys Glu Ala Lys Glu Gln His Pro Asp Met Ser Val Thr Lys
            565             570             575


Val Val Val His Gln Glu Thr Glu Ile Ala Asp Glu
            580             585
```

```
<210>   2411
<211>   982
<212>   PRT
<213>   Homo sapiens


<400>   2411
```

```
Met Ala Asn Ser Met Asn Gly Arg Asn Pro Gly Gly Arg Gly Gly Asn
1               5               10              15


Pro Arg Lys Gly Arg Ile Leu Gly Ile Ile Asp Ala Ile Gln Asp Ala
            20              25              30


Val Gly Pro Pro Lys Gln Ala Ala Ala Asp Arg Arg Thr Val Glu Lys
            35              40              45


Thr Trp Lys Leu Met Asp Lys Val Val Arg Leu Cys Gln Asn Pro Lys
    50              55              60


Leu Gln Leu Lys Asn Ser Pro Pro Tyr Ile Leu Asp Ile Leu Pro Asp
65              70              75              80


Thr Tyr Gln His Leu Arg Leu Ile Leu Ser Lys Tyr Asp Asp Asn Gln
            85              90              95


Lys Leu Ala Gln Leu Ser Glu Asn Glu Tyr Phe Lys Ile Tyr Ile Asp
            100             105             110


Ser Leu Met Lys Lys Ser Lys Arg Ala Ile Arg Leu Phe Lys Glu Gly
            115             120             125


Lys Glu Arg Met Tyr Glu Glu Gln Ser Gln Asp Arg Arg Asn Leu Thr
            130             135             140


Lys Leu Ser Leu Ile Phe Ser His Met Leu Ala Glu Ile Lys Ala Ile
145             150             155             160
```

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Phe Pro Asn Gly Gln Phe Gln Gly Asp Asn Phe Arg Ile Thr Lys Ala
             165   170   175

Asp Ala Ala Glu Phe Trp Arg Lys Phe Phe Gly Asp Lys Thr Ile Val
             180   185   190

Pro Trp Lys Val Phe Arg Gln Cys Leu His Glu Val His Gln Ile Ser
             195   200   205

Ser Gly Leu Glu Ala Met Ala Leu Lys Ser Thr Ile Asp Leu Thr Cys
     210   215   220

Asn Asp Tyr Ile Ser Val Phe Glu Phe Asp Ile Phe Thr Arg Leu Phe
225   230   235   240

Gln Pro Trp Gly Ser Ile Leu Arg Asn Trp Asn Phe Leu Ala Val Thr
             245   250   255

His Pro Gly Tyr Met Ala Phe Leu Thr Tyr Asp Glu Val Lys Ala Arg
             260   265   270

Leu Gln Lys Tyr Ser Thr Lys Pro Gly Ser Tyr Ile Phe Arg Leu Ser
             275   280   285

Cys Thr Arg Leu Gly Gln Trp Ala Ile Gly Tyr Val Thr Gly Asp Gly
     290   295   300

Asn Ile Leu Gln Thr Ile Pro His Asn Lys Pro Leu Phe Gln Ala Leu
305   310   315   320

Ile Asp Gly Ser Arg Glu Gly Phe Tyr Leu Tyr Pro Asp Gly Arg Ser
             325   330   335

Tyr Asn Pro Asp Leu Thr Gly Leu Cys Glu Pro Thr Pro His Asp His
             340   345   350

Ile Lys Val Thr Gln Glu Gln Tyr Glu Leu Tyr Cys Glu Met Gly Ser
             355   360   365

Thr Phe Gln Leu Cys Lys Ile Cys Ala Glu Asn Asp Lys Asp Val Lys
     370   375   380

Ile Glu Pro Cys Gly His Leu Met Cys Thr Ser Cys Leu Thr Ala Trp
385   390   395   400.

Gln Glu Ser Asp Gly Gln Gly Cys Pro Phe Cys Arg Cys Glu Ile Lys

```
                    405                    410                    415
```

Gly Thr Glu Pro Ile Ile Val Asp Pro Phe Asp Pro Arg Asp Glu Gly
            420   425   430

Ser Arg Cys Cys Ser Ile Ile Asp Pro Phe Gly Met Pro Met Leu Asp
            435   440   445

Leu Asp Asp Asp Asp Arg Glu Glu Ser Leu Met Met Asn Arg Leu
    450   455   460

Ala Asn Val Arg Lys Cys Thr Asp Arg Gln Asn Ser Pro Val Thr Ser
465   470   475   480

Pro Gly Ser Ser Pro Leu Ala Gln Arg Arg Lys Pro Gln Pro Asp Pro
            485   490   495

Leu Gln Ile Pro His Leu Ser Leu Pro Pro Val Pro Pro Arg Leu Asp
            500   505   510

Leu Ile Gln Lys Gly Ile Val Arg Ser Pro Cys Gly Ser Pro Thr Gly
            515   520   525

Ser Pro Lys Ser Ser Pro Cys Met Val Arg Lys Gln Asp Lys Pro Leu
    530   535   540

Pro Ala Pro Pro Pro Pro Leu Arg Asp Pro Pro Pro Pro Pro Glu
545   550   555   560

Arg Pro Pro Pro Ile Pro Pro Asp Asn Arg Leu Ser Arg His Ile His
            565   570   575

His Val Glu Ser Val Pro Ser Lys Asp Pro Pro Met Pro Leu Glu Ala
            580   585   590

Trp Cys Pro Arg Asp Val Phe Gly Thr Asn Gln Leu Val Gly Cys Arg
    595   600   605

Leu Leu Gly Glu Gly Ser Pro Lys Pro Gly Ile Thr Ala Ser Ser Asn
    610   615   620

Val Asn Gly Arg His Ser Arg Val Gly Ser Asp Pro Val Leu Met Arg
625   630   635   640

Lys His Arg Arg His Asp Leu Pro Leu Glu Gly Ala Lys Val Phe Ser
            645   650   655

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Asn Gly His Leu Gly Ser Glu Glu Tyr Asp Val Pro Pro Arg Leu Ser
        660   665   670

Pro Pro Pro Pro Val Thr Thr Leu Leu Pro Ser Ile Lys Cys Thr Gly
        675   680   685

Pro Leu Ala Asn Ser Leu Ser Glu Lys Thr Arg Asp Pro Val Glu Glu
    690   695   700

Asp Asp Asp Glu Tyr Lys Ile Pro Ser Ser His Pro Val Ser Leu Asn
705   710   715   720

Ser Gln Pro Ser His Cys His Asn Val Lys Pro Pro Val Arg Ser Cys
                725   730   735

Asp Asn Gly His Cys Met Leu Asn Gly Thr His Gly Pro Ser Ser Glu
            740   745   750

Lys Lys Ser Asn Ile Pro Asp Leu Ser Ile Tyr Leu Lys Gly Asp Val
        755   760   765

Phe Asp Ser Ala Ser Asp Pro Val Pro Leu Pro Pro Ala Arg Pro Pro
    770   775   780

Thr Arg Asp Asn Pro Lys His Gly Ser Ser Leu Asn Arg Thr Pro Ser
785   790   795   800

Asp Tyr Asp Leu Leu Ile Pro Pro Leu Gly Glu Asp Ala Phe Asp Ala
                805   810   815

Leu Pro Pro Ser Leu Pro Pro Pro Pro Pro Pro Ala Arg His Ser Leu
            820   825   830

Ile Glu His Ser Lys Pro Pro Gly Ser Ser Ser Arg Pro Ser Ser Gly
        835   840   845

Gln Asp Leu Phe Leu Leu Pro Ser Asp Pro Phe Val Asp Leu Ala Ser
    850   855   860

Gly Gln Val Pro Leu Pro Pro Ala Arg Arg Leu Pro Gly Glu Asn Val
865   870   875   880

Lys Thr Asn Arg Thr Ser Gln Asp Tyr Asp Gln Leu Pro Ser Cys Ser
                885   890   895

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```
Asp Gly Ser Gln Ala Pro Ala Arg Pro Pro Lys Pro Arg Pro Arg Arg
            900             905             910

Thr Ala Pro Glu Ile His His Arg Lys Pro His Gly Pro Glu Ala Ala
            915             920             925

Leu Glu Asn Val Asp Ala Lys Ile Ala Lys Leu Met Gly Glu Gly Tyr
            930             935             940

Ala Phe Glu Glu Val Lys Arg Ala Leu Glu Ile Ala Gln Asn Asn Val
945             950             955             960

Glu Val Ala Arg Ser Ile Leu Arg Glu Phe Ala Phe Pro Pro Pro Val
            965             970             975

Ser Pro Arg Leu Asn Leu
            980


<210>   2412
<211>   352
<212>   PRT
<213>   Homo sapiens

<400>   2412

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
1               5               10              15

Ser Glu Pro Cys Gln Lys Ile Asn Val Lys Gln Ile Ala Ala Arg Leu
            20              25              30

Leu Pro Pro Leu Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn
            35              40              45

Met Leu Val Ile Leu Ile Leu Ile Asn Cys Lys Arg Leu Lys Ser Met
    50              55              60

Thr Asp Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp Leu Phe Phe Leu
65              70              75              80

Leu Thr Val Pro Phe Trp Ala His Tyr Ala Ala Ala Gln Trp Asp Phe
            85              90              95

Gly Asn Thr Met Cys Gln Leu Leu Thr Gly Leu Tyr Phe Ile Gly Phe
            100             105             110

Phe Ser Gly Ile Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu
```

```
            115                    120                    125


Ala Val Val His Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe
    130                    135                140


Gly Val Val Thr Ser Val Ile Thr Trp Val Val Ala Val Phe Ala Ser
145                    150                155                160


Leu Pro Gly Ile Ile Phe Thr Arg Ser Gln Lys Glu Gly Leu His Tyr
                165                170                175


Thr Cys Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn
            180                185                190


Phe Gln Thr Leu Lys Ile Val Ile Leu Gly Leu Val Leu Pro Leu Leu
            195                200                205


Val Met Val Ile Cys Tyr Ser Gly Ile Leu Lys Thr Leu Leu Arg Cys
    210                    215                220


Arg Asn Glu Lys Lys Arg His Arg Ala Val Arg Leu Ile Phe Thr Ile
225                    230                235                240


Met Ile Val Tyr Phe Leu Phe Trp Ala Pro Tyr Asn Ile Val Leu Leu
                245                250                255
                             I

Leu Asn Thr Phe Gln Glu Phe Phe Gly Leu Asn Asn Cys Ser Ser Ser
            260                265                270


Asn Arg Leu Asp Gln Ala Met Gln Val Thr Glu Thr Leu Gly Met Thr
            275                280                285


His Cys Cys Ile Asn Pro Ile Ile Tyr Ala Phe Val Gly Glu Lys Phe
    290                    295                300


Arg Asn Tyr Leu Leu Val Phe Phe Gln Lys His Ile Ala Lys Arg Phe
305                    310                315                320


Cys Lys Cys Cys Ser Ile Phe Gln Gln Glu Ala Pro Glu Arg Ala Ser
            325                330                335


Ser Val Tyr Thr Arg Ser Thr Gly Glu Gln Glu Ile Ser Val Gly Leu
            340                345              , 350


<210> 2413
<211> 750
```

<212>   PRT
<213>   Homo sapiens

<400>   2413

Met Gly Lys Ser Glu Ser Gln Met Asp Ile Thr Asp Ile Asn Thr Pro
1   5   10   15

Lys Pro Lys Lys Lys Gln Arg Trp Thr Arg Leu Glu Ile Ser Leu Ser
            20   25   30

Val Leu Val Leu Leu Leu Thr Ile Ile Ala Val Arg Met Ile Ala Leu
        35   40   45

Tyr Ala Thr Tyr Asp Asp Gly Ile Cys Lys Ser Ser Asp Cys Ile Lys
    50   55   60

Ser Ala Ala Arg Leu Ile Gln Asn Met Asp Ala Thr Thr Glu Pro Cys
65   70   75   80

Arg Asp Phe Phe Lys Tyr Ala Cys Gly Gly Trp Leu Lys Arg Asn Val
            85   90   95

Ile Pro Glu Thr Ser Ser Arg Tyr Gly Asn Phe Asp Ile Leu Arg Asp
            100   105   110

Glu Leu Glu Val Val Leu Lys Asp Val Leu Gln Glu Pro Lys Thr Glu
        115   120   125

Asp Ile Val Ala Val Gln Lys Ala Lys Ala Leu Tyr Arg Ser Cys Ile
    130   135   140

Asn Glu Ser Ala Ile Asp Ser Arg Gly Gly Glu Pro Leu Leu Lys Leu
145   150   155   160

Leu Pro Asp Ile Tyr Gly Trp Pro Val Ala Thr Glu Asn Trp Glu Gln
            165   170   175

Lys Tyr Gly Ala Ser Trp Thr Ala Glu Lys Ala Ile Ala Gln Leu Asn
            180   185   190

Ser Lys Tyr Gly Lys Lys Val Leu Ile Asn Leu Phe Val Gly Thr Asp
    195   200   205

Asp Lys Asn Ser Val Asn His Val Ile His Ile Asp Gln Pro Arg Leu
    210   215   220

```
Gly Leu Pro Ser Arg Asp Tyr Tyr Glu Cys Thr Gly Ile Tyr Lys Glu
225                 230             235                 240


Ala Cys Thr Ala Tyr Val Asp Phe Met Ile Ser Val Ala Arg Leu Ile
                245             250                 255


Arg Gln Glu Glu Arg Leu Pro Ile Asp Glu Asn Gln Leu Ala Leu Glu
            260             265                 270


Met Asn Lys Val Met Glu Leu Glu Lys Glu Ile Ala Asn Ala Thr Ala
        275             280                 285


Lys Pro Glu Asp Arg Asn Asp Pro Met Leu Leu Tyr Asn Lys Met Arg
    290             295             300


Leu Ala Gln Ile Gln Asn Asn Phe Ser Leu Glu Ile Asn Gly Lys Pro
305                 310             315                 320


Phe Ser Trp Leu Asn Phe Thr Asn Glu Ile Met Ser Thr Val Asn Ile
                325             330                 335


Ser Ile Thr Asn Glu Glu Asp Val Val Val Tyr Ala Pro Glu Tyr Leu
            340             345                 350


Thr Lys Leu Lys Pro Ile Leu Thr Lys Tyr Ser Ala Arg Asp Leu Gln
        355             360                 365


Asn Leu Met Ser Trp Arg Phe Ile Met Asp Leu Val Ser Ser Leu Ser
    370             375             380


Arg Thr Tyr Lys Glu Ser Arg Asn Ala Phe Arg Lys Ala Leu Tyr Gly
385                 390             395                 400


Thr Thr Ser Glu Thr Ala Thr Trp Arg Arg Cys Ala Asn Tyr Val Asn
                405             410                 415


Gly Asn Met Glu Asn Ala Val Gly Arg Leu Tyr Val Glu Ala Ala Phe
            420             425                 430


Ala Gly Glu Ser Lys His Val Val Glu Asp Leu Ile Ala Gln Ile Arg
        435             440                 445


Glu Val Phe Ile Gln Thr Leu Asp Asp Leu Thr Trp Met Asp Ala Glu
    450             455             460


Thr Lys Lys Arg Ala Glu Glu Lys Ala Leu Ala Ile Lys Glu Arg Ile
```

Gly Tyr Pro Asp Asp Ile Val Ser Asn Asp Asn Lys Leu Asn Asn Glu
            485   490   495

Tyr Leu Glu Leu Asn Tyr Lys Glu Asp Glu Tyr Phe Glu Asn Ile Ile
            500   505   510

Gln Asn Leu Lys Phe Ser Gln Ser Lys Gln Leu Lys Lys Leu Arg Glu
            515   520   525

Lys Val Asp Lys Asp Glu Trp Ile Ser Gly Ala Ala Val Val Asn Ala
            530   535   540   °

Phe Tyr Ser Ser Gly Arg Asn Gln Ile Val Phe Pro Ala Gly Ile Leu
545   550   555   560

Gln Pro Pro Phe Phe Ser Ala Gln Gln Ser Asn Ser Leu Asn Tyr Gly
            565   570   575

Gly Ile Gly Met Val Ile Gly His Glu Ile Thr His Gly Phe Asp Asp
            580   585   590

Asn Gly Arg Asn Phe Asn Lys Asp Gly Asp Leu Val Asp Trp Trp Thr
            595   600   605

Gln Gln Ser Ala Ser Asn Phe Lys Glu Gln Ser Gln Cys Met Val Tyr
            610   615   620

Gln Tyr Gly Asn Phe Ser Trp Asp Leu Ala Gly Gly Gln His Leu Asn
625   630   635   640

Gly Ile Asn Thr Leu Gly Glu Asn Ile Ala Asp Asn Gly Gly Leu Gly
            645   650   655

Gln Ala Tyr Arg Ala Tyr Gln Asn Tyr Ile Lys Lys Asn Gly Glu Glu
            660   665   670

Lys Leu Leu Pro Gly Leu Asp Leu Asn His Lys Gln Leu Phe Phe Leu
            675   680   685

Asn Phe Ala Gln Val Trp Cys Gly Thr Tyr Arg Pro Glu Tyr Ala Val
            690   695   700

Asn Ser Ile Lys Thr Asp Val His Ser Pro Gly Asn Phe Arg Ile Ile
705   710   715   720

702

```
Gly Thr Leu Gln Asn Ser Ala Glu Phe Ser Glu Ala Phe His Cys Arg
            725                 730                 735

Lys Asn Ser Tyr Met Asn Pro Glu Lys Lys Cys Arg Val Trp
            740                 745                 750
```

```
<210>    2414
<211>    233
<212>    PRT
<213>    Homo sapiens

<400>    2414
```

```
Met Asp Asn Gln Gly Val Ile Tyr Ser Asp Leu Asn Leu Pro Pro Asn
1               5               10                  15

Pro Lys Arg Gln Gln Arg Lys Pro Lys Gly Asn Lys Ser Ser Ile Leu
            20              25                  30

Ala Thr Glu Gln Glu Ile Thr Tyr Ala Glu Leu Asn Leu Gln Lys Ala
        35              40                  45

Ser Gln Asp Phe Gln Gly Asn Asp Lys Thr Tyr His Cys Lys Asp Leu
    50              55                  60

Pro Ser Ala Pro Glu Lys Leu Ile Val Gly Ile Leu Gly Ile Ile Cys
65              70                  75                  80

Leu Ile Leu Met Ala Ser Val Val Thr Ile Val Val Ile Pro Ser Thr
                85              90                  95

Leu Ile Gln Arg His Asn Asn Ser Ser Leu Asn Thr Arg Thr Gln Lys
            100             105                 110

Ala Arg His Cys Gly His Cys Pro Glu Glu Trp Ile Thr Tyr Ser Asn
        115             120                 125

Ser Cys Tyr Tyr Ile Gly Lys Glu Arg Arg Thr Trp Glu Glu Ser Leu
    130             135                 140

Leu Ala Cys Thr Ser Lys Asn Ser Ser Leu Leu Ser Ile Asp Asn Glu
145             150                 155                 160

Glu Glu Met Lys Phe Leu Ser Ile Ile Ser Pro Ser Ser Trp Ile Gly
            165             170                 175
```

Val Phe Arg Asn Ser Ser His His Pro Trp Val Thr Met Asn Gly Leu
        180   185   190

Ala Phe Lys His Glu Ile Lys Asp Ser Asp Asn Ala Glu Leu Asn Cys
        195   200   205

Ala Val Leu Gln Val Asn Arg Leu Lys Ser Ala Gln Cys Gly Ser Ser
    210   215   220

Ile Ile Tyr His Cys Lys His Lys Leu
225   230

<210> 2415
<211> 290
<212> PRT
<213> Homo sapiens

<400> 2415

Met Gly Gly Gly Ala Gly Glu Arg Leu Phe Thr Ser Ser Cys Leu Val
1   5   10   15

Gly Leu Val Pro Leu Gly Leu Arg Ile Ser Leu Val Thr Cys Pro Leu
            20   25   30

Gln Cys Gly Ile Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu
        35   40   45

Leu Val Ser Ala Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val
    50   55   60

Phe Leu Glu Pro Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr
65   70   75   80

Leu Lys Cys Gln Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp
            85   90   95

Phe His Asn Glu Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile
        100   105   110

Asp Ala Ala Thr Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn
        115   120   125

Leu Ser Thr Leu Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp
    130   135   140

Leu Leu Leu Gln Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile
145   150   155   160

704

His Leu Arg Cys His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr
            165   170   175

Tyr Leu Gln Asn Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp
            180   185   190

Phe Tyr Ile Pro Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys
            195   200   205

Arg Gly Leu Val Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile
    210   215   220

Thr Ile Thr Gln Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro
225   230   235   240

Pro Gly Tyr Gln Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala
            245   250   255

Val Asp Thr Gly Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser
            260   265   270

Thr Arg Asp Trp Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln
            275   280   285

Asp Lys
    290

<210> 2416
<211> 233
<212> PRT
<213> Homo sapiens

<400> 2416

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1   5   10   15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20   25   30

Gln Trp Tyr Ser Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
            35   40   45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50   55   60

```
Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65              70              75              80


Val Asn Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
            85              90              95


Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
        100             105             110


Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
    115             120             125


His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130             135             140


Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145             150             155             160


Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
            165             170             175


Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180             185             190


Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195             200             205


Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210             215             220


Leu Tyr Phe Ser Val Lys Thr Asn Ile
225             230
```

```
<210>  2417
<211>  525
<212>  PRT
<213>  Homo sapiens

<400>  2417

Met Trp Glu Ala Gln Phe Leu Gly Leu Leu Phe Leu Gln Pro Leu Trp
1               5               10              15


Val Ala Pro Val Lys Pro Leu Gln Pro Gly Ala Glu Val Pro Val Val
            20              25              30


Trp Ala Gln Glu Gly Ala Pro Ala Gln Leu Pro Cys Ser Pro Thr Ile
        35              40              45
```

706

```
Pro Leu Gln Asp Leu Ser Leu Leu Arg Arg Ala Gly Val Thr Trp Gln
    50                  55                  60


His Gln Pro Asp Ser Gly Pro Pro Ala Ala Ala Pro Gly His Pro Leu
65                  70                  75                  80


Ala Pro Gly Pro His Pro Ala Ala Pro Ser Ser Trp Gly Pro Arg Pro
                85                  90                  95


Arg Arg Tyr Thr Val Leu Ser Val Gly Pro Gly Gly Leu Arg Ser Gly
            100                 105                 110


Arg Leu Pro Leu Gln Pro Arg Val Gln Leu Asp Glu Arg Gly Arg Gln
        115                 120                 125


Arg Gly Asp Phe Ser Leu Trp Leu Arg Pro Ala Arg Arg Ala Asp Ala
    130                 135                 140


Gly Glu Tyr Arg Ala Ala Val His Leu Arg Asp Arg Ala Leu Ser Cys
145                 150                 155                 160


Arg Leu Arg Leu Arg Leu Gly Gln Ala Ser Met Thr Ala Ser Pro Pro
            165                 170                 175


Gly Ser Leu Arg Ala Ser Asp Trp Val Ile Leu Asn Cys Ser Phe Ser
        180                 185                 190


Arg Pro Asp Arg Pro Ala Ser Val His Trp Phe Arg Asn Arg Gly Gln
    195                 200                 205


Gly Arg Val Pro Val Arg Glu Ser Pro His His His Leu Ala Glu Ser
210                 215                 220


Phe Leu Phe Leu Pro Gln Val Ser Pro Met Asp Ser Gly Pro Trp Gly
225                 230                 235                 240


Cys Ile Leu Thr Tyr Arg Asp Gly Phe Asn Val Ser Ile Met Tyr Asn
            245                 250                 255


Leu Thr Val Leu Gly Leu Glu Pro Pro Thr Pro Leu Thr Val Tyr Ala
            260                 265                 270


Gly Ala Gly Ser Arg Val Gly Leu Pro Cys Arg Leu Pro Ala Gly Val
    275                 280                 285
```

707

Gly Thr Arg Ser Phe Leu Thr Ala Lys Trp Thr Pro Pro Gly Gly Gly
    290   295   300

Pro Asp Leu Leu Val Thr Gly Asp Asn Gly Asp Phe Thr Leu Arg Leu
305   310   315   320

Glu Asp Val Ser Gln Ala Gln Ala Gly Thr Tyr Thr Cys His Ile His
            325   330   335

Leu Gln Glu Gln Gln Leu Asn Ala Thr Val Thr Leu Ala Ile Ile Thr
            340   345   350

Val Thr Pro Lys Ser Phe Gly Ser Pro Gly Ser Leu Gly Lys Leu Leu
            355   360   365

Cys Glu Val Thr Pro Val Ser Gly Gln Glu Arg Phe Val Trp Ser Ser
    370   375   -   380

Leu Asp Thr Pro Ser Gln Arg Ser Phe Ser Gly Pro Trp Leu Glu Ala
385   390   395   400

Gln Glu Ala Gln Leu Leu Ser Gln Pro Trp Gln Cys Gln Leu Tyr Gln
            405   410   415

Gly Glu Arg Leu Leu Gly Ala Ala Val Tyr Phe Thr Glu Leu Ser Ser
            420   425   430

Pro Gly Ala Gln Arg Ser Gly Arg Ala Pro Gly Ala Leu Pro Ala Gly
            435   440   445

His Leu Leu Leu Phe Leu Thr Leu Gly Val Leu Ser Leu Leu Leu Leu
            450   455   460

Val Thr Gly Ala Phe Gly Phe His Leu Trp Arg Arg Gln Trp Arg Pro
465   470   475   480

Arg Arg Phe Ser Ala Leu Glu Gln Gly Ile His Pro Pro Gln Ala Gln
            485   490   495

Ser Lys Ile Glu Glu Leu Glu Gln Glu Pro Glu Pro Glu Pro Glu Pro
            500   505   510

Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro Glu Gln Leu
            515   520   525

<210> 2418
<211> 738
<212> PRT
<213> Homo sapiens

<400> 2418

Met Gln Pro Arg Trp Ala Gln Gly Ala Thr Met Trp Leu Gly Val Leu
1   5   10   15

Leu Thr Leu Leu Leu Cys Ser Ser Leu Glu Gly Gln Glu Asn Ser Phe
            20   25   30

Thr Ile Asn Ser Val Asp Met Lys Ser Leu Pro Asp Trp Thr Val Gln
        35   40   45

Asn Gly Lys Asn Leu Thr Leu Gln Cys Phe Ala Asp Val Ser Thr Thr
    50   55   60

Ser His Val Lys Pro Gln His Gln Met Leu Phe Tyr Lys Asp Asp Val
65   70   75   80

Leu Phe Tyr Asn Ile Ser Ser Met Lys Ser Thr Glu Ser Tyr Phe Ile
                85   90   95

Pro Glu Val Arg Ile Tyr Asp Ser Gly Thr Tyr Lys Cys Thr Val Ile
            100   105   110

Val Asn Asn Lys Glu Lys Thr Thr Ala Glu Tyr Gln Val Leu Val Glu
            115   120   125

Gly Val Pro Ser Pro Arg Val Thr Leu Asp Lys Lys Glu Ala Ile Gln
    130   135   140

Gly Gly Ile Val Arg Val Asn Cys Ser Val Pro Glu Glu Lys Ala Pro
145   150   155   160

Ile His Phe Thr Ile Glu Lys Leu Glu Leu Asn Glu Lys Met Val Lys
                165   170   175

Leu Lys Arg Glu Lys Asn Ser Arg Asp Gln Asn Phe Val Ile Leu Glu
            180   185   190

Phe Pro Val Glu Glu Gln Asp Arg Val Leu Ser Phe Arg Cys Gln Ala
            195   200   205

Arg Ile Ile Ser Gly Ile His Met Gln Thr Ser Glu Ser Thr Lys Ser
    210   215   220

709

Glu Leu Val Thr Val Thr Glu Ser Phe Ser Thr Pro Lys Phe His Ile
225   230   235   240

Ser Pro Thr Gly Met Ile Met Glu Gly Ala Gln Leu His Ile Lys Cys
                245   250   255

Thr Ile Gln Val Thr His Leu Ala Gln Glu Phe Pro Glu Ile Ile Ile
                260   265   270

Gln Lys Asp Lys Ala Ile Val Ala His Asn Arg His Gly Asn Lys Ala
                275   280   285

Val Tyr Ser Val Met Ala Met Val Glu His Ser Gly Asn Tyr Thr Cys
290   295   300

Lys Val Glu Ser Ser Arg Ile Ser Lys Val Ser Ser Ile Val Val Asn
305   310   315   320

Ile Thr Glu Leu Phe Ser Lys Pro Glu Leu Glu Ser Ser Phe Thr His
                325   330   335

Leu Asp Gln Gly Glu Arg Leu Asn Leu Ser Cys Ser Ile Pro Gly Ala
                340   345   350

Pro Pro Ala Asn Phe Thr Ile Gln Lys Glu Asp Thr Ile Val Ser Gln
                355   360   365

Thr Gln Asp Phe Thr Lys Ile Ala Ser Lys Ser Asp Ser Gly Thr Tyr
                370   375   380

Ile Cys Thr Ala Gly Ile Asp Lys Val Val Lys Lys Ser Asn Thr Val
385   390   395   400

Gln Ile Val Val Cys Glu Met Leu Ser Gln Pro Arg Ile Ser Tyr Asp
                405   410   415

Ala Gln Phe Glu Val Ile Lys Gly Gln Thr Ile Glu Val Arg Cys Glu
                420   425   430

Ser Ile Ser Gly Thr Leu Pro Ile Ser Tyr Gln Leu Leu Lys Thr Ser
                435   440   445

Lys Val Leu Glu Asn Ser Thr Lys Asn Ser Asn Asp Pro Ala Val Phe
                450   455   460

```
Lys Asp Asn Pro Thr Glu Asp Val Glu Tyr Gln Cys Val Ala Asp Asn
465              470              475                   480

Cys His Ser His Ala Lys Met Leu Ser Glu Val Leu Arg Val Lys Val
            485              490                   495

Ile Ala Pro Val Asp Glu Val Gln Ile Ser Ile Leu Ser Ser Lys Val
        500              505                   510

Val Glu Ser Gly Glu Asp Ile Val Leu Gln Cys Ala Val Asn Glu Gly
        515              520                   525

Ser Gly Pro Ile Thr Tyr Lys Phe Tyr Arg Glu Lys Glu Gly Lys Pro
    530              535              540

Phe Tyr Gln Met Thr Ser Asn Ala Thr Gln Ala Phe Trp Thr Lys Gln
545              550              555                   560

Lys Ala Asn Lys Glu Gln Glu Gly Glu Tyr Tyr Cys Thr Ala Phe Asn
            565              570                   575

Arg Ala Asn His Ala Ser Ser Val Pro Arg Ser Lys Ile Leu Thr Val
        580              585              590

Arg Val Ile Leu Ala Pro Trp Lys Lys Gly Leu Ile Ala Val Val Ile
    595              600              605

Ile Gly Val Ile Ile Ala Leu Leu Ile Ile Ala Ala Lys Cys Tyr Phe
    610              615              620

Leu Arg Lys Ala Lys Ala Lys Gln Met Pro Val Glu Met Ser Arg Pro
625              630              635                   640

Ala Val Pro Leu Leu Asn Ser Asn Asn Glu Lys Met Ser Asp Pro Asn
            645              650                   655

Met Glu Ala Asn Ser His Tyr Gly His Asn Asp Asp Val Gly Asn His
            660              665                   670

Ala Met Lys Pro Ile Asn Asp Asn Lys Glu Pro Leu Asn Ser Asp Val
        675              680                   685

Gln Tyr Thr Glu Val Gln Val Ser Ser Ala Glu Ser His Lys Asp Leu
    690              695                   700
```

711

```
Gly Lys Lys Asp Thr Glu Thr Val Tyr Ser Glu Val Arg Lys Ala Val
705             710             715             720


Pro Asp Ala Val Glu Ser Arg Tyr Ser Arg Thr Glu Gly Ser Leu Asp
            725             730             735


Gly Thr



<210>  2419
<211>  328
<212>  PRT
<213>  Homo sapiens

<400>  2419

Met Leu Val Arg Arg Gly Ala Arg Ala Gly Pro Arg Met Pro Arg Gly
1               5               10              15


Trp Thr Ala Leu Cys Leu Leu Ser Leu Leu Pro Ser Gly Phe Met Ser
            20              25              30


Leu Asp Asn Asn Gly Thr Ala Thr Pro Glu Leu Pro Thr Gln Gly Thr
            35              40              45


Phe Ser Asn Val Ser Thr Asn Val Ser Tyr Gln Glu Thr Thr Thr Pro
        50              55              60


Ser Thr Leu Gly Ser Thr Ser Leu His Pro Val Ser Gln His Gly Asn
65              70              75              80


Glu Ala Thr Thr Asn Ile Thr Glu Thr Thr Val Lys Phe Thr Ser Thr
                85              90              95


Ser Val Ile Thr Ser Val Tyr Gly Asn Thr Asn Ser Ser Val Gln Ser
            100             105             110


Gln Thr Ser Val Ile Ser Thr Val Phe Thr Thr Pro Ala Asn Val Ser
        115             120             125


Thr Pro Glu Thr Thr Leu Lys Pro Ser Leu Ser Pro Gly Asn Val Ser
        130             135             140


Asp Leu Ser Thr Thr Ser Thr Ser Leu Ala Thr Ser Pro Thr Lys Pro
145             150             155             160


Tyr Thr Ser Ser Ser Pro Ile Leu Ser Asp Ile Lys Ala Glu Ile Lys
                165             170             175
```

Cys Ser Gly Ile Arg Glu Val Lys Leu Thr Gln Gly Ile Cys Leu Glu
            180   185   190

Gln Asn Lys Thr Ser Ser Cys Ala Glu Phe Lys Lys Asp Arg Gly Glu
            195   200   205

Gly Leu Ala Arg Val Leu Cys Gly Glu Glu Gln Ala Asp Ala Asp Ala
            210   215   220

Gly Ala Gln Val Cys Ser Leu Leu Leu Ala Gln Ser Glu Val Arg Pro
225   230   235   240

Gln Cys Leu Leu Leu Val Leu Ala Asn Arg Thr Glu Ile Ser Ser Lys
                245   250   255

Leu Gln Leu Met Lys Lys His Gln Ser Asp Leu Lys Lys Leu Gly Ile
            260   265   270

Leu Asp Phe Thr Glu Gln Asp Val Ala Ser His Gln Ser Tyr Ser Gln
            275   280   285

Lys Thr Leu Ile Ala Leu Val Thr Ser Gly Ala Leu Leu Ala Val Leu
290   295   300

Gly Ile Thr Gly Tyr Phe Leu Met Asn Arg Arg Ser Trp Ser Pro Thr
305   310   315   320

Gly Glu Arg Leu Glu Leu Glu Pro
            325

<210> 2420
<211> 374
<212> PRT
<213> Homo sapiens

<400> 2420

Met Trp Phe Leu Thr Thr Leu Leu Leu Trp Val Pro Val Asp Gly Gln
1   5   10   15

Val Asp Thr Thr Lys Ala Val Ile Thr Leu Gln Pro Pro Trp Val Ser
            20   25   30

Val Phe Gln Glu Glu Thr Val Thr Leu His Cys Glu Val Leu His Leu
            35   40   45

```
Pro Gly Ser Ser Ser Thr Gln Trp Phe Leu Asn Gly Thr Ala Thr Gln
    50              55                  60


Thr Ser Thr Pro Ser Tyr Arg Ile Thr Ser Ala Ser Val Asn Asp Ser
65              70                  75                  80
                .


Gly Glu Tyr Arg Cys Gln Arg Gly Leu Ser Gly Arg Ser Asp Pro Ile
            85                  90                  95


Gln Leu Glu Ile His Arg Gly Trp Leu Leu Leu Gln Val Ser Ser Arg
            100                 105                 110


Val Phe Thr Glu Gly Glu Pro Leu Ala Leu Arg Cys His Ala Trp Lys
        115                 120                 125


Asp Lys Leu Val Tyr Asn Val Leu Tyr Tyr Arg Asn Gly Lys Ala Phe
    130                 135                 140


Lys Phe Phe His Trp Asn Ser Asn Leu Thr Ile Leu Lys Thr Asn Ile
145                 150                 155                 160


Ser His Asn Gly Thr Tyr His Cys Ser Gly Met Gly Lys His Arg Tyr
            165                 170                 175


Thr Ser Ala Gly Ile Ser Val Thr Val Lys Glu Leu Phe Pro Ala Pro
        180                 185                 190


Val Leu Asn Ala Ser Val Thr Ser Pro Leu Leu Glu Gly Asn Leu Val
        195                 200                 205


Thr Leu Ser Cys Glu Thr Lys Leu Leu Leu Gln Arg Pro Gly Leu Gln
210                 215                 220


Leu Tyr Phe Ser Phe Tyr Met Gly Ser Lys Thr Leu Arg Gly Arg Asn
225                 230                 235                 240


Thr Ser Ser Glu Tyr Gln Ile Leu Thr Ala Arg Arg Glu Asp Ser Gly
            245                 250                 255


Leu Tyr Trp Cys Glu Ala Ala Thr Glu Asp Gly Asn Val Leu Lys Arg
        260                 265                 270


Ser Pro Glu Leu Glu Leu Gln Val Leu Gly Leu Gln Leu Pro Thr Pro
    275                 280                 285


Val Trp Phe His Val Leu Phe Tyr Leu Ala Val Gly Ile Met Phe Leu
```

714

```
            290                  295                  300


Val Asn Thr Val Leu Trp Val Thr Ile Arg Lys Glu Leu Lys Arg Lys
305                 310                 315                 320


Lys Lys Trp Asp Leu Glu Ile Ser Leu Asp Ser Gly His Glu Lys Lys
                325                 330                 335


Val Ile Ser Ser Leu Gln Glu Asp Arg His Leu Glu Glu Glu Leu Lys
                340                 345                 350


Cys Gln Glu Gln Lys Glu Glu Gln Leu Gln Glu Gly Val His Arg Lys
                355                 360                 365


Glu Pro Gln Gly Ala Thr
        370


<210>   2421
<211>   760
<212>   PRT
<213>   Homo sapiens

<400>   2421

Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu
1                   5                   10                  15


Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp
                20                  25                  30


Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala
        35                  40                  45


Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly
    50                  55                  60


Ser Ile Cys Tyr Gly Thr Ile Ala Val Ile Val Phe Phe Leu Ile Gly
65                  70                  75                  80


Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr
                85                  90                  95


Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro
                100                 105                 110


Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys
                115                 120                 125
```

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Ser Thr Ile
    130   135   140

Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln
145   150   155   160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe
              165   170   175

Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val
          180   185   190

Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg
          195   200   205

Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys
    210   215   220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys
225   230   235   240

Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile
              245   250   255

Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu
          260   265   270

Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe
          275   280   285

Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly
    290   295   300

Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln
305   310   315   320

Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr
              325   330   335

Ile Ser Arg Ala Ala Ala Glu Lys Leu Phe Gly Asn Met Glu Gly Asp
          340   345   350

Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser
          355   360   365

716

Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile
    370   375   380

Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp
385   390   395   400

His Tyr Val Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala
                405   410   415

Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Leu Lys Leu Ala Gln Met
            420   425   430

Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile
            435   440   445

Ile Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr
    450   455   460

Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr
465   470   475   480

Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val
            485   490   495

Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn
            500   505   510

Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp
    515   520   525

Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe
    530   535   540

Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp
545   550   555   560

Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu
            565   570   575

Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Ala Glu
            580   585   590

Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn
    595   600   605

Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp

                                    717

```
      610                      615                    620
```

```
Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln
625                 630             635                     640
```

```
Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu
                645             650                     655
```

```
Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys
            660             665                 670
```

```
Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro
        675                 680             685
```

```
Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser
    690                 695             700
```

```
Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys
705                 710             715                     720
```

```
Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala
            725             730                     735
```

```
Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
            740             745                 750
```

```
Val Trp Asp Ile Asp Asn Glu Phe
        755             760
```

```
<210>  2422
<211>  247
<212>  PRT
<213>  Homo sapiens

<400>  2422
```

```
Met Leu Leu Leu Pro Leu Pro Leu Leu Leu Phe Leu Leu Cys Ser Arg
1               5               10              15
```

```
Ala Glu Ala Gly Glu Ile Ile Gly Gly Thr Glu Cys Lys Pro His Ser
            20              25              30
```

```
Arg Pro Tyr Met Ala Tyr Leu Glu Ile Val Thr Ser Asn Gly Pro Ser
    35              40              45
```

```
Lys Phe Cys Gly Gly Phe Leu Ile Arg Arg Asn Phe Val Leu Thr Ala
    50              55              60
```

Ala His Cys Ala Gly Arg Ser Ile Thr Val Thr Leu Gly Ala His Asn
65   70   75   80

Ile Thr Glu Glu Glu Asp Thr Trp Gln Lys Leu Glu Val Ile Lys Gln
                85   90   95

Phe Arg His Pro Lys Tyr Asn Thr Ser Thr Leu His His Asp Ile Met
            100   105   110

Leu Leu Lys Leu Lys Glu Lys Ala Ser Leu Thr Leu Ala Val Gly Thr
            115   120   125

Leu Pro Phe Pro Ser Gln Phe Asn Phe Val Pro Pro Gly Arg Met Cys
    130   135   140

Arg Val Ala Gly Trp Gly Arg Thr Gly Val Leu Lys Pro Gly Ser Asp
145   150   155   160

Thr Leu Gln Glu Val Lys Leu Arg Leu Met Asp Pro Gln Ala Cys Ser
            165   170   175

His Phe Arg Asp Phe Asp His Asn Leu Gln Leu Cys Val Gly Asn Pro
            180   185   190

Arg Lys Thr Lys Ser Ala Phe Lys Gly Asp Ser Gly Gly Pro Leu Leu
            195   200   205

Cys Ala Gly Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Ser Asp Ala
    210   215   220

Lys Pro Pro Ala Val Phe Thr Arg Ile Ser His Tyr Arg Pro Trp Ile
225   230   235   240

Asn Gln Ile Leu Gln Ala Asn
                245

<210>   2423
<211>   976
<212>   PRT
<213>   Homo sapiens

<400>   2423

Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
1   5   10   15

Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly

```
                    20                      25                      30

    Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
            35              40              45

    Arg Val Gly Asp Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
            50              55              60

    Lys Trp Thr Phe Glu Ile Leu Asp Glu Thr Asn Glu Asn Lys Gln Asn
    65              70              75              80

    Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
                    85              90              95

    Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
                    100             105             110

    Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
                    115             120             125

    Asp Asn Asp Thr Leu Val Arg Cys Pro Leu Thr Asp Pro Glu Val Thr
            130             135             140

    Asn Tyr Ser Leu Lys Gly Cys Gln Gly Lys Pro Leu Pro Lys Asp Leu
    145             150             155             160

    Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
                    165             170             175

    Arg Ala Tyr His Arg Leu Cys Leu His Cys Ser Val Asp Gln Glu Gly
                    180             185             190

    Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
            195             200             205

    Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg
            210             215             220

    Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
    225             230             235             240

    Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
                    245             250             255

    Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
            260             265             270
```

Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
        275   280   285

Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
290   295   300

Leu Glu Val Val Asp Lys Gly Phe Ile Asn Ile Phe Pro Met Ile Asn
305   310   315   320

Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
            325   330   335

Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
            340   345   350

Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
            355   360   365

Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
    370   375   380

Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385   390   395   400

Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Lys Pro Glu Ile Leu
            405   410   415

Thr Tyr Asp Arg Leu Val Asn Gly Met Leu Gln Cys Val Ala Ala Gly
            420   425   430

Phe Pro Glu Pro Thr Ile Asp Trp Tyr Phe Cys Pro Gly Thr Glu Gln
            435   440   445

Arg Cys Ser Ala Ser Val Leu Pro Val Asp Val Gln Thr Leu Asn Ser
    450   455   460

Ser Gly Pro Pro Phe Gly Lys Leu Val Val Gln Ser Ser Ile Asp Ser
465   470   475   480

Ser Ala Phe Lys His Asn Gly Thr Val Glu Cys Lys Ala Tyr Asn Asp
            485   490   495

Val Gly Lys Thr Ser Ala Tyr Phe Asn Phe Ala Phe Lys Gly Asn Asn
        500   505   510

721

```
Lys Glu Gln Ile His Pro His Thr Leu Phe Thr Pro Leu Leu Ile Gly
        515             520             525

Phe Val Ile Val Ala Gly Met Met Cys Ile Ile Val Met Ile Leu Thr
    530             535             540

Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln Trp Lys Val Val
545             550             555             560

Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp Pro Thr Gln Leu
                565             570             575

Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg Leu Ser Phe Gly
            580             585             590

Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
        595             600             605

Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val Ala Val Lys Met
    610             615             620

Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala Leu Met Ser Glu
625             630             635             640

Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn Ile Val Asn Leu
                645             650             655

Leu Gly Ala Cys Thr Ile Gly Gly Pro Thr Leu Val Ile Thr Glu Tyr
            660             665             670

Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Arg Asp Ser
        675             680             685

Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala Ala Leu Tyr Lys
    690             695             700

Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp Ser Thr Asn Glu
705             710             715             720

Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val Pro Thr Lys Ala
            725             730             735

Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile Glu Arg Asp Val
        740             745             750
```

722

```
Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu Asp Leu Glu Asp
        755             760             765

Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met Ala Phe Leu Ala
        770             775             780

Ser Lys Asn Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu
785             790             795             800

Thr His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp
                805             810             815

Ile Lys Asn Asp Ser Asn Tyr Val Val Lys Gly Asn Ala Arg Leu Pro
            820             825             830

Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Cys Val Tyr Thr Phe
        835             840             845

Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp Glu Leu Phe Ser
    850             855             860

Leu Gly Ser Ser Pro Tyr Pro Gly Met Pro Val Asp Ser Lys Phe Tyr
865             870             875             880

Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro Glu His Ala Pro
            885             890             895

Ala Glu Met Tyr Asp Ile Met Lys Thr Cys Trp Asp Ala Asp Pro Leu
        900             905             910

Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile Glu Lys Gln Ile
        915             920             925

Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala Asn Cys Ser Pro
    930             935             940

Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg Ile Asn Ser Val
945             950             955             960

Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val His Asp Asp Val
            965             970             975
```

```
<210>  2424
<211>  635
<212>  PRT
<213>  Homo sapiens
```

<400> 2424

Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1   5   10   15

Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
            20   25   30

Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
        35   40   45

Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
    50   55   60

Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65   70   75   80

Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
                85   90   95

Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
            100   105   110

Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
            115   120   125

Ser Val Gly Leu Pro Ala Pro Pro Ser Ile Ile Lys Ala Met Gly Gly
        130   135   140

Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145   150   155   160

Ile Ser Asp Phe Leu Arg Tyr Glu Leu Arg Tyr Gly Pro Arg Asp Pro
                165   170   175

Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
            180   185   190

Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
        195   200   205

Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
    210   215   220

Thr Ser Pro Ser Arg Glu Ala Ser Ala Leu Thr Ala Glu Gly Gly Ser
225   230   235   240

```
Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
             245             250             255


Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
             260             265             270


Ser Leu Pro Val Thr Val Asp Leu Pro Gly Asp Ala Val Ala Leu Gly
             275             280             285


Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
     290             295             300


Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305             310             315             320


Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
             325             330             335


Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
             340             345             350


His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
             355             360             365


Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
     370             375             380


Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385             390             395             400


Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
             405             410             415


Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
             420             425             430


Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
             435             440             445


Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
     450             455             460


Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp Ser Asp Pro
465             470             475             480
```

```
Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr
              485             490             495
```

```
Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
            500             505             510
```

```
Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
        515             520             525
```

```
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
    530             535             540
```

```
Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
545             550             555             560
```

```
Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
            565             570             575
```

```
Arg Thr Pro Leu Pro Leu Cys Ser Ser Gln Ala Gln Met Asp Tyr Arg
        580             585             590
```

```
Arg Leu Gln Pro Ser Cys Leu Gly Thr Met Pro Leu Ser Val Cys Pro
        595             600             605
```

```
Pro Met Ala Glu Ser Gly Ser Cys Cys Thr Thr His Ile Ala Asn His
    610             615             620
```

```
Ser Tyr Leu Pro Leu Ser Tyr Trp Gln Gln Pro
625             630             635
```

```
<210>  2425
<211>  1006
<212>  PRT
<213>  Homo sapiens

<400>  2425
```

```
Met Val Cys Ser Leu Trp Val Leu Leu Val Ser Ser Val Leu Ala
1               5               10              15
```

```
Leu Glu Glu Val Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly
            20              25              30
```

```
Trp Leu Thr Tyr Pro Pro Gly Gly Trp Asp Glu Val Ser Val Leu Asp
        35              40              45
```

```
Asp Gln Arg Arg Leu Thr Arg Thr Phe Glu Ala Cys His Val Ala Gly
    50              55              60
```

Ala Pro Pro Gly Thr Gly Gln Asp Asn Trp Leu Gln Thr His Phe Val
65   70   75   80

Glu Arg Arg Gly Ala Gln Arg Ala His Ile Arg Leu His Phe Ser Val
                85   90   95

Arg Ala Cys Ser Ser Leu Gly Val Ser Gly Gly Thr Cys Arg Glu Thr
            100   105   110

Phe Thr Leu Tyr Tyr Arg Gln Ala Glu Glu Pro Asp Ser Pro Asp Ser
        115   120   125

Val Ser Ser Trp His Leu Lys Arg Trp Thr Lys Val Asp Thr Ile Ala
    130   135   140

Ala Asp Glu Ser Phe Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
145   150   155   160

Ser Ala Ala Trp Ala Val Gly Pro His Gly Ala Gly Gln Arg Ala Gly
            165   170   175

Leu Gln Leu Asn Val Lys Glu Arg Ser Phe Gly Pro Leu Thr Gln Arg
            180   185   190

Gly Phe Tyr Val Ala Phe Gln Asp Thr Gly Ala Cys Leu Ala Leu Val
        195   200   205

Ala Val Arg Leu Phe Ser Tyr Thr Cys Pro Ala Val Leu Arg Ser Phe
210   215   220

Ala Ser Phe Pro Glu Thr Gln Ala Ser Gly Ala Gly Gly Ala Ser Leu
225   230   235   240

Val Ala Ala Val Gly Thr Cys Val Ala His Ala Glu Pro Glu Glu Asp
            245   250   255

Gly Val Gly Gly Gln Ala Gly Gly Ser Pro Pro Arg Leu His Cys Asn
            260   265   270

Gly Glu Gly Lys Trp Met Val Ala Val Gly Gly Cys Arg Cys Gln Pro
        275   280   285

Gly Tyr Gln Pro Ala Arg Gly Asp Lys Ala Cys Gln Ala Cys Pro Arg
    290   295   300

727

```
Gly Leu Tyr Lys Ser Ser Ala Gly Asn Ala Pro Cys Ser Pro Cys Pro
305             310             315                 320

Ala Arg Ser His Ala Pro Asn Pro Ala Ala Pro Val Cys Pro Cys Leu
            325             330                 335

Glu Gly Phe Tyr Arg Ala Ser Ser Asp Pro Pro Glu Ala Pro Cys Thr
            340             345                 350

Gly Pro Pro Ser Ala Pro Gln Glu Leu Trp Phe Glu Val Gln Gly Ser
        355             360                 365

Ala Leu Met Leu His Trp Arg Leu Pro Arg Glu Leu Gly Gly Arg Gly
    370             375                 380

Asp Leu Leu Phe Asn Val Val Cys Lys Glu Cys Glu Gly Arg Gln Glu
385             390             395                 400

Pro Ala Ser Gly Gly Gly Gly Thr Cys His Arg Cys Arg Asp Glu Val
            405             410                 415

His Phe Asp Pro Arg Gln Arg Gly Leu Thr Glu Ser Arg Val Leu Val
            420             425                 430

Gly Gly Leu Arg Ala His Val Pro Tyr Ile Leu Glu Val Gln Ala Val
        435             440                 445

Asn Gly Val Ser Glu Leu Ser Pro Asp Pro Pro Gln Ala Ala Ala Ile
  ·450             455                 460

Asn Val Ser Thr Ser His Glu Val Pro Ser Ala Val Pro Val Val His
465             470             475                 480

Gln Val Ser Arg Ala Ser Asn Ser Ile Thr Val Ser Trp Pro Gln Pro
            485             490                 495

Asp Gln Thr Asn Gly Asn Ile Leu Asp Tyr Gln Leu Arg Tyr Tyr Asp
            500             505                 510

Gln Ala Glu Asp Glu Ser His Ser Phe Thr Leu Thr Ser Glu Thr Asn
            515             520                 525

Thr Ala Thr Val Thr Gln Leu Ser Pro Gly His Ile Tyr Gly Phe Gln
    530             535                 540
```

Val Arg Ala Arg Thr Ala Ala Gly His Gly Pro Tyr Gly Gly Lys Val
545   550   555   560

Tyr Phe Gln Thr Leu Pro Gln Gly Glu Leu Ser Ser Gln Leu Pro Glu
                565   570   575

Arg Leu Ser Leu Val Ile Gly Ser Ile Leu Gly Ala Leu Ala Phe Leu
                580   585   590

Leu Leu Ala Ala Ile Thr Val Leu Ala Val Val Phe Gln Arg Lys Arg
                595   600   605

Arg Gly Thr Gly Tyr Thr Glu Gln Leu Gln Gln Tyr Ser Ser Pro Gly
610   615   620

Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Cys
625   630   635   640

Gln Ala Ile Arg Glu Leu Ala Arg Glu Val Asp Pro Ala Tyr Ile Lys
                645   650   655

Ile Glu Glu Val Ile Gly Thr Gly Ser Phe Gly Glu Val Arg Gln Gly
                660   665   670

Arg Leu Gln Pro Arg Gly Arg Arg Glu Gln Thr Val Ala Ile Gln Ala
                675   680   685

Leu Trp Ala Gly Gly Ala Glu Ser Leu Gln Met Thr Phe Leu Gly Arg
                690   695   700

Ala Ala Val Leu Gly Gln Phe Gln His Pro Asn Ile Leu Arg Leu Glu
705   710   715   720

Gly Val Val Thr Lys Ser Arg Pro Leu Met Val Leu Thr Glu Phe Met
                725   730   735

Glu Leu Gly Pro Leu Asp Ser Phe Leu Arg Gln Arg Glu Gly Gln Phe
                740   745   750

Ser Ser Leu Gln Leu Val Ala Met Gln Arg Gly Val Ala Ala Ala Met
                755   760   765

Gln Tyr Leu Ser Ser Phe Ala Phe Val His Arg Ser Leu Ser Ala His
770   775   780

Ser Val Leu Val Asn Ser His Leu Val Cys Lys Val Ala Arg Leu Gly

729

```
        785              790                   795                   800
```

```
   His Ser Pro Gln Gly Pro Ser Cys Leu Leu Arg Trp Ala Ala Pro Glu
                805                   810                   815
```

```
   Val Ile Ala His Gly Lys His Thr Thr Ser Ser Asp Val Trp Ser Phe
                820                   825                   830
```

```
   Gly Ile Leu Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
                835                   840                   845
```

```
   Asp Met Ser Glu Gln Glu Val Leu Asn Ala Ile Glu Gln Glu Phe Arg
       850                   855                   860
```

```
   Leu Pro Pro Pro Pro Gly Cys Pro Pro Gly Leu His Leu Leu Met Leu
   865                   870                   875                   880
```

```
   Asp Thr Trp Gln Lys Asp Arg Ala Arg Arg Pro His Phe Asp Gln Leu
                885                   890                   895
```

```
   Val Ala Ala Phe Asp Lys Met Ile Arg Lys Pro Asp Thr Leu Gln Ala
                900                   905                   910
```

```
   Gly Gly Asp Pro Gly Glu Arg Pro Ser Gln Ala Leu Leu Thr Pro Val
                915                   920                   925
```

```
   Ala Leu Asp Phe Pro Cys Leu Asp Ser Pro Gln Ala Trp Leu Ser Ala
       930                   935                   940
```

```
   Ile Gly Leu Glu Cys Tyr Gln Asp Asn Phe Ser Lys Phe Gly Leu Cys
   945                   950                   955                   960
```

```
   Thr Phe Ser Asp Val Ala Gln Leu Ser Leu Glu Asp Leu Pro Ala Leu
                965                   970                   975
```

```
   Gly Ile Thr Leu Ala Gly His Gln Lys Lys Leu Leu His His Ile Gln
                980                   985                   990
```

```
   Leu Leu Gln Gln His Leu Arg Gln  Gln Gly Ser Val Glu  Val
       995                   1000                  1005
```

<210> 2426
<211> 508
<212> PRT
<213> Homo sapiens

<400> 2426

```
Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5               10                  15


Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20              25                  30


Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35              40                  45


Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50              55                  60


Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65              70              75                  80


Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
            85                  90                  95


Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100             105                 110


Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115             120                 125


Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130             135             140


Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145             150             155                 160


His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165             170                 175


His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
            180             185             190


Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195             200             205


Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210             215             220


Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225             230             235                 240
```

731

Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
            245   250   255

Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
            260   265   270

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
        275   280   285

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
    290   295   300

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
305   310   315   320

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
            325   330   335

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
            340   345   350

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
        355   360   365

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
370   375   380

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
385   390   395   400

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
            405   410   415

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
            420   425   430

Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
        435   440   445

Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
    450   455   460

Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
465   470   475   480

Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala

732

                    485   490   495

        Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
                    500   505

        <210> 2427
        <211> 441
        <212> PRT
        <213> Homo sapiens

        <400> 2427

        Met Ser Pro Ile Ser Gly Ala Ser Pro Ser Trp Arg Ala Ala Pro Lys
        1   5   10   15

        Ala Ser Asp Leu Leu Gly Ala Arg Gly Pro Gly Gly Thr Phe Gln Gly
                    20   25   30

        Arg Asp Leu Arg Gly Gly Ala His Ala Ser Ser Ser Ser Leu Asn Pro
                    35   40   45

        Met Pro Pro Ser Gln Leu Gln Leu Ser Thr Val Asp Ala His Ala Arg
            50   55   60

        Thr Pro Val Leu Gln Val His Pro Leu Glu Ser Pro Ala Met Ile Ser
        65   70   75   80

        Leu Thr Pro Pro Thr Thr Ala Thr Gly Val Phe Ser Leu Lys Ala Arg
                        85   90   95

        Pro Gly Leu Pro Pro Gly Ile Asn Val Ala Ser Leu Glu Trp Val Ser
                    100   105   110

        Arg Glu Pro Ala Leu Leu Cys Thr Phe Pro Asn Pro Ser Ala Pro Arg
                    115   120   125

        Lys Asp Ser Thr Leu Ser Ala Val Pro Gln Ser Ser Tyr Pro Leu Leu
            130   135   140

        Ala Asn Gly Val Cys Lys Trp Pro Gly Cys Glu Lys Val Phe Glu Glu
        145   150   155   160

        Pro Glu Asp Phe Leu Lys His Cys Gln Ala Asp His Leu Leu Asp Glu
                        165   170   175

        Lys Gly Arg Ala Gln Cys Leu Leu Gln Arg Glu Met Val Gln Ser Leu
                    180   185   190

```
Glu Gln Gln Leu Val Leu Glu Lys Glu Lys Leu Ser Ala Met Gln Ala
        195             200             205

His Leu Ala Gly Lys Met Ala Leu Thr Lys Ala Ser Ser Val Ala Ser
    210             215             220

Ser Asp Lys Gly Ser Cys Cys Ile Val Ala Ala Gly Ser Gln Gly Pro
225             230             235             240

Val Val Pro Ala Trp Ser Gly Pro Arg Glu Ala Pro Asp Ser Leu Phe
            245             250             255

Ala Val Arg Arg His Leu Trp Gly Ser His Gly Asn Ser Thr Phe Pro
        260             265             270

Glu Phe Leu His Asn Met Asp Tyr Phe Lys Phe His Asn Met Arg Pro
    275                 280             285

Pro Phe Thr Tyr Ala Thr Leu Ile Arg Trp Ala Ile Leu Glu Ala Pro
    290             295             300

Glu Lys Gln Arg Thr Leu Asn Glu Ile Tyr His Trp Phe Thr Arg Met
305             310             315             320

Phe Ala Phe Phe Arg Asn His Pro Ala Thr Trp Lys Val Ser Ser Ser
            325             330             335

Glu Val Ala Val Thr Gly Met Ala Ser Ser Ala Ile Ala Ala Gln Ser
            340             345             350

Gly Gln Ala Trp Val Trp Ala His Arg His Ile Gly Glu Glu Arg Asp
        355             360             365

Val Gly Cys Trp Trp Trp Leu Leu Ala Ser Glu Val Asp Ala His Leu
    370             375             380

Leu Pro Val Pro Gly Leu Pro Gln Asn Ala Ile Arg His Asn Leu Ser
385             390             395             400

Leu His Lys Cys Phe Val Arg Val Glu Ser Glu Lys Gly Ala Val Trp
            405             410             415

Thr Val Asp Glu Leu Glu Phe Arg Lys Lys Arg Ser Gln Arg Pro Ser
            420             425             430
```

Arg Cys Ser Asn Pro Thr Pro Gly Pro
        435   440

<210> 2428
<211> 413
<212> PRT
<213> Homo sapiens

<400> 2428

Met Glu Phe Pro Gly Leu Gly Ser Leu Gly Thr Ser Glu Pro Leu Pro
1   5   10   15

Gln Phe Val Asp Pro Ala Leu Val Ser Ser Thr Pro Glu Ser Gly Val
            20   25   30

Phe Phe Pro Ser Gly Pro Glu Gly Leu Asp Ala Ala Ala Ser Ser Thr
        35   40   45

Ala Pro Ser Thr Ala Thr Ala Ala Ala Ala Leu Ala Tyr Tyr Arg
    50   55   60

Asp Ala Glu Ala Tyr Arg His Ser Pro Val Phe Gln Val Tyr Pro Leu
65   70   75   80

Leu Asn Cys Met Glu Gly Ile Pro Gly Gly Ser Pro Tyr Ala Gly Trp
            85   90   95

Ala Tyr Gly Lys Thr Gly Leu Tyr Pro Ala Ser Thr Val Cys Pro Thr
            100   105   110

Arg Glu Asp Ser Pro Pro Gln Ala Val Glu Asp Leu Asp Gly Lys Gly
            115   120   125

Ser Thr Ser Phe Leu Glu Thr Leu Lys Thr Glu Arg Leu Ser Pro Asp
    130   135   140

Leu Leu Thr Leu Gly Pro Ala Leu Pro Ser Ser Leu Pro Val Pro Asn
145   150   155   160

Ser Ala Tyr Gly Gly Pro Asp Phe Ser Ser Thr Phe Phe Ser Pro Thr
            165   170   175

Gly Ser Pro Leu Asn Ser Ala Ala Tyr Ser Ser Pro Lys Leu Arg Gly
            180   185   190

Thr Leu Pro Leu Pro Pro Cys Glu Ala Arg Glu Cys Val Asn Cys Gly
            195   200   205

735

```
Ala Thr Ala Thr Pro Leu Trp Arg Arg Asp Arg Thr Gly His Tyr Leu
    210                 215             220

Cys Asn Ala Cys Gly Leu Tyr His Lys Met Asn Gly Gln Asn Arg Pro
225                 230             235                 240

Leu Ile Arg Pro Lys Lys Arg Leu Ile Val Ser Lys Arg Ala Gly Thr
                245             250                 255

Gln Cys Thr Asn Cys Gln Thr Thr Thr Thr Leu Trp Arg Arg Asn
                260             265                 270

Ala Ser Gly Asp Pro Val Cys Asn Ala Cys Gly Leu Tyr Tyr Lys Leu
                275             280             285

His Gln Val Asn Arg Pro Leu Thr Met Arg Lys Asp Gly Ile Gln Thr
    290                 295             300

Arg Asn Arg Lys Ala Ser Gly Lys Gly Lys Lys Lys Arg Gly Ser Ser
305                 310             315                 320

Leu Gly Gly Thr Gly Ala Ala Glu Gly Pro Ala Gly Gly Phe Met Val
                325             330             335

Val Ala Gly Gly Ser Gly Ser Gly Asn Cys Gly Glu Val Ala Ser Gly
                340             345             350

Leu Thr Leu Gly Pro Pro Gly Thr Ala His Leu Tyr Gln Gly Leu Gly
                355             360             365

Pro Val Val Leu Ser Gly Pro Val Ser His Leu Met Pro Phe Pro Gly
    370                 375             380

Pro Leu Leu Gly Ser Pro Thr Gly Ser Phe Pro Thr Gly Pro Met Pro
385                 390             395                 400

Pro Thr Thr Ser Thr Thr Val Val Ala Pro Leu Ser Ser
                405             410
```

```
<210>  2429
<211>  1039
<212>  PRT
<213>  Homo sapiens

<400>  2429
```

```
Met Ala Arg Ala Leu Cys Pro Leu Gln Ala Leu Trp Leu Leu Glu Trp
1               5                   10              15

Val Leu Leu Leu Leu Gly Pro Cys Ala Ala Pro Pro Ala Trp Ala Leu
            20                  25                  30

Asn Leu Asp Pro Val Gln Leu Thr Phe Tyr Ala Gly Pro Asn Gly Ser
        35                  40                  45

Gln Phe Gly Phe Ser Leu Asp Phe His Lys Asp Ser His Gly Arg Val
    50                  55                  60

Ala Ile Val Val Gly Ala Pro Arg Thr Leu Gly Pro Ser Gln Glu Glu
65                  70                  75                  80

Thr Gly Gly Val Phe Leu Cys Pro Trp Arg Ala Glu Gly Gly Gln Cys
                85                  90                  95

Pro Ser Leu Leu Phe Asp Leu Arg Asp Glu Thr Arg Asn Val Gly Ser
            100                 105                 110

Gln Thr Leu Gln Thr Phe Lys Ala Arg Gln Gly Leu Gly Ala Ser Val
        115                 120                 125

Val Ser Trp Ser Asp Val Ile Val Ala Cys Ala Pro Trp Gln His Trp
    130                 135                 140

Asn Val Leu Glu Lys Thr Glu Glu Ala Glu Lys Thr Pro Val Gly Ser
145                 150                 155                 160

Cys Phe Leu Ala Gln Pro Glu Ser Gly Arg Arg Ala Glu Tyr Ser Pro
            165                 170                 175

Cys Arg Gly Asn Thr Leu Ser Arg Ile Tyr Val Glu Asn Asp Phe Ser
            180                 185                 190

Trp Asp Lys Arg Tyr Cys Glu Ala Gly Phe Ser Ser Val Val Thr Gln
        195                 200                 205

Ala Gly Glu Leu Val Leu Gly Ala Pro Gly Gly Tyr Tyr Phe Leu Gly
    210                 215                 220

Leu Leu Ala Gln Ala Pro Val Ala Asp Ile Phe Ser Ser Tyr Arg Pro
225                 230                 235                 240

Gly Ile Leu Leu Trp His Val Ser Ser Gln Ser Leu Ser Phe Asp Ser
```

737

                    245   250   255

        Ser Asn Pro Glu Tyr Phe Asp Gly Tyr Trp Gly Tyr Ser Val Ala Val
                    260   265   270

        Gly Glu Phe Asp Gly Asp Leu Asn Thr Thr Glu Tyr Val Val Gly Ala
                    275   280   285

        Pro Thr Trp Ser Trp Thr Leu Gly Ala Val Glu Ile Leu Asp Ser Tyr
            290   295   300

        Tyr Gln Arg Leu His Arg Leu Arg Ala Glu Gln Met Ala Ser Tyr Phe
        305   310   315   320

        Gly His Ser Val Ala Val Thr Asp Val Asn Gly Asp Gly Arg His Asp
                    325   330   335

        Leu Leu Val Gly Ala Pro Leu Tyr Met Glu Ser Arg Ala Asp Arg Lys
                    340   345   350

        Leu Ala Glu Val Gly Arg Val Tyr Leu Phe Leu Gln Pro Arg Gly Pro
                    355   360   365

        His Ala Leu Gly Ala Pro Ser Leu Leu Leu Thr Gly Thr Gln Leu Tyr
            370   375   380

        Gly Arg Phe Gly Ser Ala Ile Ala Pro Leu Gly Asp Leu Asp Arg Asp
        385   390   395   400

        Gly Tyr Asn Asp Ile Ala Val Ala Ala Pro Tyr Gly Gly Pro Ser Gly
                        405   410   415

        Arg Gly Gln Val Leu Val Phe Leu Gly Gln Ser Glu Gly Leu Arg Ser
                    420   425   430

        Arg Pro Ser Gln Val Leu Asp Ser Pro Phe Pro Thr Gly Ser Ala Phe
                    435   440   445

        Gly Phe Ser Leu Arg Gly Ala Val Asp Ile Asp Asp Asn Gly Tyr Pro
            450   455   460

        Asp Leu Ile Val Gly Ala Tyr Gly Ala Asn Gln Val Ala Val Tyr Arg
        465   470   475   480

        Ala Gln Pro Val Val Lys Ala Ser Val Gln Leu Leu Val Gln Asp Ser
                        485   490   495

```
Leu Asn Pro Ala Val Lys Ser Cys Val Leu Pro Gln Thr Lys Thr Pro
        500             505             510


Val Ser Cys Phe Asn Ile Gln Met Cys Val Gly Ala Thr Gly His Asn
        515             520             525


Ile Pro Gln Lys Leu Ser Leu Asn Ala Glu Leu Gln Leu Asp Arg Gln
    530             535             540


Lys Pro Arg Gln Gly Arg Arg Val Leu Leu Leu Gly Ser Gln Gln Ala
545             550             555             560


Gly Thr Thr Leu Asn Leu Asp Leu Gly Gly Lys His Ser Pro Ile Cys
            565             570             575


His Thr Thr Met Ala Phe Leu Arg Asp Glu Ala Asp Phe Arg Asp Lys
        580             585             590


Leu Ser Pro Ile Val Leu Ser Leu Asn Val Ser Leu Pro Pro Thr Glu
        595             600             605


Ala Gly Met Ala Pro Ala Val Val Leu His Gly Asp Thr His Val Gln
    610             615             620


Glu Gln Thr Arg Ile Val Leu Asp Ser Gly Glu Asp Asp Val Cys Val
625             630             635             640


Pro Gln Leu Gln Leu Thr Ala Ser Val Thr Gly Ser Pro Leu Leu Val
            645             650             655


Gly Ala Asp Asn Val Leu Glu Leu Gln Met Asp Ala Ala Asn Glu Gly
            660             665             670


Glu Gly Ala Tyr Glu Ala Glu Leu Ala Val His Leu Pro Gln Gly Ala
        675             680             685


His Tyr Met Arg Ala Leu Ser Asn Val Glu Gly Phe Glu Arg Leu Ile
    690             695             700


Cys Asn Gln Lys Lys Glu Asn Glu Thr Arg Val Val Leu Cys Glu Leu
705             710             715             720


Gly Asn Pro Met Lys Lys Asn Ala Gln Ile Gly Ile Ala Met Leu Val
            725             730             735
```

Ser Val Gly Asn Leu Glu Glu Ala Gly Glu Ser Val Ser Phe Gln Leu
        740   745   750

Gln Ile Arg Ser Lys Asn Ser Gln Asn Pro Asn Ser Lys Ile Val Leu
        755   760   765

Leu Asp Val Pro Val Arg Ala Glu Ala Gln Val Glu Leu Arg Gly Asn
    770   775   780

Ser Phe Pro Ala Ser Leu Val Val Ala Ala Glu Glu Gly Glu Arg Glu
785   790   795   800

Gln Asn Ser Leu Asp Ser Trp Gly Pro Lys Val Glu His Thr Tyr Glu
            805   810   815

Leu His Asn Asn Gly Pro Gly Thr Val Asn Gly Leu His Leu Ser Ile
            820   825   830

His Leu Pro Gly Gln Ser Gln Pro Ser Asp Leu Leu Tyr Ile Leu Asp
    835   840   845

Ile Gln Pro Gln Gly Gly Leu Gln Cys Phe Pro Gln Pro Pro Val Asn
    850   855   860

Pro Leu Lys Val Asp Trp Gly Leu Pro Ile Pro Ser Pro Ser Pro Ile
865   870   875   880

His Pro Ala His His Lys Arg Asp Arg Arg Gln Ile Phe Leu Pro Glu
            885   890   895

Pro Glu Gln Pro Ser Arg Leu Gln Asp Pro Val Leu Val Ser Cys Asp
        900   905   910

Ser Ala Pro Cys Thr Val Val Gln Cys Asp Leu Gln Glu Met Ala Arg
        915   920   925

Gly Gln Arg Ala Met Val Thr Val Leu Ala Phe Leu Trp Leu Pro Ser
    930   935   940

Leu Tyr Gln Arg Pro Leu Asp Gln Phe Val Leu Gln Ser His Ala Trp
945   950   955   960

Phe Asn Val Ser Ser Leu Pro Tyr Ala Val Pro Pro Leu Ser Leu Pro
            965   970   975

Arg Gly Glu Ala Gln Val Trp Thr Gln Leu Leu Arg Ala Leu Glu Glu
          980   985   990

Arg Ala Ile Pro Ile Trp Trp Val Leu Val Gly Val Leu Gly Gly Leu
          995   1000   1005

Leu Leu Leu Thr Ile Leu Val Leu Ala Met Trp Lys Val Gly Phe
     1010   1015   1020

Phe Lys Arg Asn Arg Pro Pro Leu Glu Glu Asp Asp Glu Glu Gly
     1025   1030   1035

Glu

<210>   2430
<211>   145
<212>   PRT
<213>   Homo sapiens

<400>   2430

Met Ala Thr Trp Ala Leu Leu Leu Leu Ala Ala Met Leu Leu Gly Asn
1   5   10   15

Pro Gly Leu Val Phe Ser Arg Leu Ser Pro Glu Tyr Tyr Asp Leu Ala
          20   25   30

Arg Ala His Leu Arg Asp Glu Glu Lys Ser Cys Pro Cys Leu Ala Gln
          35   40   45

Glu Gly Pro Gln Gly Asp Leu Leu Thr Lys Thr Gln Glu Leu Gly Arg
     50   55   60

Asp Tyr Arg Thr Cys Leu Thr Ile Val Gln Lys Leu Lys Lys Met Val
65   70   75   80

Asp Lys Pro Thr Gln Arg Ser Val Ser Asn Ala Ala Thr Arg Val Cys
               85   90   95

Arg Thr Gly Arg Ser Arg Trp Arg Asp Val Cys Arg Asn Phe Met Arg
               100   105   110

Arg Tyr Gln Ser Arg Val Thr Gln Gly Leu Val Ala Gly Glu Thr Ala
          115   120   125

Gln Gln Ile Cys Glu Asp Leu Arg Leu Cys Ile Pro Ser Thr Gly Pro
          130   135   140

Leu
145

<210>   2431
<211>   262
<212>   PRT
<213>   Homo sapiens

<400>   2431

Met Arg Asn Ser Tyr Arg Phe Leu Ala Ser Ser Leu Ser Val Val Val
1   5   10   15

Ser Leu Leu Leu Ile Pro Glu Asp Val Cys Glu Lys Ile Ile Gly Gly
            20   25   30

Asn Glu Val Thr Pro His Ser Arg Pro Tyr Met Val Leu Leu Ser Leu
            35   40   45

Asp Arg Lys Thr Ile Cys Ala Gly Ala Leu Ile Ala Lys Asp Trp Val
        50   55   60

Leu Thr Ala Ala His Cys Asn Leu Asn Lys Arg Ser Gln Val Ile Leu
65   70   75   80

Gly Ala His Ser Ile Thr Arg Glu Glu Pro Thr Lys Gln Ile Met Leu
                85   90   95

Val Lys Lys Glu Phe Pro Tyr Pro Cys Tyr Asp Pro Ala Thr Arg Glu
            100   105   110

Gly Asp Leu Lys Leu Leu Gln Leu Thr Glu Lys Ala Lys Ile Asn Lys
            115   120   125

Tyr Val Thr Ile Leu His Leu Pro Lys Lys Gly Asp Asp Val Lys Pro
    130   135   140

Gly Thr Met Cys Gln Val Ala Gly Trp Gly Arg Thr His Asn Ser Ala
145   150   155   160

Ser Trp Ser Asp Thr Leu Arg Glu Val Asn Ile Thr Ile Ile Asp Arg
                165   170   175

Lys Val Cys Asn Asp Arg Asn His Tyr Asn Phe Asn Pro Val Ile Gly
                180   185   190

```
Met Asn Met Val Cys Ala Gly Ser Leu Arg Gly Gly Arg Asp Ser Cys
        195              200              205

Asn Gly Asp Ser Gly Ser Pro Leu Leu Cys Glu Gly Val Phe Arg Gly
    210              215              220

Val Thr Ser Phe Gly Leu Glu Asn Lys Cys Gly Asp Pro Arg Gly Pro
225              230              235              240

Gly Val Tyr Ile Leu Leu Ser Lys Lys His Leu Asn Trp Ile Ile Met
            245              250              255

Thr Ile Lys Gly Ala Val
            260
```

```
<210>  2432
<211>  142
<212>  PRT
<213>  Homo sapiens

<400>  2432
```

```
Met Val Leu Ser Pro Ala Asp Lys Thr Asn Val Lys Ala Ala Trp Gly
1             5              10              15

Lys Val Gly Ala His Ala Gly Glu Tyr Gly Ala Glu Ala Leu Glu Arg
        20              25              30

Met Phe Leu Ser Phe Pro Thr Thr Lys Thr Tyr Phe Pro His Phe Asp
        35              40              45

Leu Ser His Gly Ser Ala Gln Val Lys Gly His Gly Lys Lys Val Ala
    50              55              60

Asp Ala Leu Thr Asn Ala Val Ala His Val Asp Asp Met Pro Asn Ala
65              70              75              80

Leu Ser Ala Leu Ser Asp Leu His Ala His Lys Leu Arg Val Asp Pro
            85              90              95

Val Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala
            100             105             110

His Leu Pro Ala Glu Phe Thr Pro Ala Val His Ala Ser Leu Asp Lys
        115             120             125

Phe Leu Ala Ser Val Ser Thr Val Leu Thr Ser Lys Tyr Arg
    130             135             140
```

```
<210>  2433
<211>  142
<212>  PRT
<213>  Homo sapiens

<400>  2433
```

Met Ser Leu Thr Lys Thr Glu Arg Thr Ile Ile Val Ser Met Trp Ala
1   5   10   15

Lys Ile Ser Thr Gln Ala Asp Thr Ile Gly Thr Glu Thr Leu Glu Arg
            20   25   30

Leu Phe Leu Ser His Pro Gln Thr Lys Thr Tyr Phe Pro His Phe Asp
        35   40   45

Leu His Pro Gly Ser Ala Gln Leu Arg Ala His Gly Ser Lys Val Val
    50   55   60

Ala Ala Val Gly Asp Ala Val Lys Ser Ile Asp Asp Ile Gly Gly Ala
65   70   75   80

Leu Ser Lys Leu Ser Glu Leu His Ala Tyr Ile Leu Arg Val Asp Pro
                85   90   95

Val Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala
            100   105   110

Arg Phe Pro Ala Asp Phe Thr Ala Glu Ala His Ala Ala Trp Asp Lys
        115   120   125

Phe Leu Ser Val Val Ser Ser Val Leu Thr Glu Lys Tyr Arg
    130   135   140

```
<210>  2434
<211>  147
<212>  PRT
<213>  Homo sapiens

<400>  2434
```

Met Val His Leu Thr Pro Glu Glu Lys Thr Ala Val Asn Ala Leu Trp
1   5   10   15

Gly Lys Val Asn Val Asp Ala Val Gly Gly Glu Ala Leu Gly Arg Leu
            20   25   30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Glu Ser Phe Gly Asp

```
          35                    40                    45
```

```
Leu Ser Ser Pro Asp Ala Val Met Gly Asn Pro Lys Val Lys Ala His
    50                  55                  60
```

```
Gly Lys Lys Val Leu Gly Ala Phe Ser Asp Gly Leu Ala His Leu Asp
65                  70                  75                  80
```

```
Asn Leu Lys Gly Thr Phe Ser Gln Leu Ser Glu Leu His Cys Asp Lys
                85                  90                  95
```

```
Leu His Val Asp Pro Glu Asn Phe Arg Leu Leu Gly Asn Val Leu Val
            100                 105                 110
```

```
Cys Val Leu Ala Arg Asn Phe Gly Lys Glu Phe Thr Pro Gln Met Gln
        115                 120                 125
```

```
Ala Ala Tyr Gln Lys Val Val Ala Gly Val Ala Asn Ala Leu Ala His
    130                 135                 140
```

```
Lys Tyr His
145
```

```
<210>  2435
<211>  147
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2435
```

```
Met Val His Phe Thr Ala Glu Glu Lys Ala Ala Val Thr Ser Leu Trp
1               5                   10                  15
```

```
Ser Lys Met Asn Val Glu Glu Ala Gly Gly Glu Ala Leu Gly Arg Leu
            20                  25                  30
```

```
Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Asp Ser Phe Gly Asn
        35                  40                  45
```

```
Leu Ser Ser Pro Ser Ala Ile Leu Gly Asn Pro Lys Val Lys Ala His
    50                  55                  60
```

```
Gly Lys Lys Val Leu Thr Ser Phe Gly Asp Ala Ile Lys Asn Met Asp
65                  70                  75                  80
```

```
Asn Leu Lys Pro Ala Phe Ala Lys Leu Ser Glu Leu His Cys Asp Lys
                85                  90                  95
```

```
Leu His Val Asp Pro Glu Asn Phe Lys Leu Leu Gly Asn Val Met Val
             100                 105                 110

Ile Ile Leu Ala Thr His Phe Gly Lys Glu Phe Thr Pro Glu Val Gln
         115                 120                 125

Ala Ala Trp Gln Lys Leu Val Ser Ala Val Ala Ile Ala Leu Ala His
     130                 135                 140

Lys Tyr His
145
```

```
<210>  2436
<211>  147
<212>  PRT
<213>  Homo sapiens

<400>  2436
```

```
Met Gly His Phe Thr Glu Glu Asp Lys Ala Thr Ile Thr Ser Leu Trp
1               5                   10                  15

Gly Lys Val Asn Val Glu Asp Ala Gly Gly Glu Thr Leu Gly Arg Leu
         20                  25                  30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Asp Ser Phe Gly Asn
     35                  40                  45

Leu Ser Ser Ala Ser Ala Ile Met Gly Asn Pro Lys Val Lys Ala His
     50                  55                  60

Gly Lys Lys Val Leu Thr Ser Leu Gly Asp Ala Thr Lys His Leu Asp
65                  70                  75                  80

Asp Leu Lys Gly Thr Phe Ala Gln Leu Ser Glu Leu His Cys Asp Lys
                 85                  90                  95

Leu His Val Asp Pro Glu Asn Phe Lys Leu Leu Gly Asn Val Leu Val
             100                 105                 110

Thr Val Leu Ala Ile His Phe Gly Lys Glu Phe Thr Pro Glu Val Gln
         115                 120                 125

Ala Ser Trp Gln Lys Met Val Thr Ala Val Ala Ser Ala Leu Ser Ser
     130                 135                 140

Arg Tyr His
```

145

```
<210>  2437
<211>  142
<212>  PRT
<213>  Homo sapiens

<400>  2437
```

Met Ala Leu Ser Ala Glu Asp Arg Ala Leu Val Arg Ala Leu Trp Lys
1   5   10   15

Lys Leu Gly Ser Asn Val Gly Val Tyr Thr Thr Glu Ala Leu Glu Arg
            20   25   30

Thr Phe Leu Ala Phe Pro Ala Thr Lys Thr Tyr Phe Ser His Leu Asp
        35   40   45

Leu Ser Pro Gly Ser Ser Gln Val Arg Ala His Gly Gln Lys Val Ala
    50   55   60

Asp Ala Leu Ser Leu Ala Val Glu Arg Leu Asp Asp Leu Pro His Ala
65   70   75   80

Leu Ser Ala Leu Ser His Leu His Ala Cys Gln Leu Arg Val Asp Pro
                85   90   95

Ala Ser Phe Gln Leu Leu Gly His Cys Leu Leu Val Thr Leu Ala Arg
            100   105   110

His Tyr Pro Gly Asp Phe Ser Pro Ala Leu Gln Ala Ser Leu Asp Lys
        115   120   125

Phe Leu Ser His Val Ile Ser Ala Leu Val Ser Glu Tyr Arg
    130   135   140

```
<210>  2438
<211>  260
<212>  PRT
<213>  Homo sapiens

<400>  2438
```

Met Arg Pro Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg
1   5   10   15

Ala Leu Ser Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile
            20   25   30

```
Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg
        35              40              45


Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr
        50              55              60


Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly
65              70              75              80


Gln Ala Phe Ser Phe Glu Ala Gln Gly Gly Leu Ala Asn Ile Ala Ile
            85              90              95


Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln
        100             105             110


Ala Thr Asn Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val
        115             120             125


Glu Leu Gly Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe
    130             135             140


Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr
145             150             155             160


Glu Gly Val Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe
            165             170             175


His Lys Phe His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr
            180             185             190


Asp Cys Arg Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His
        195             200             205


Trp Glu Ala Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val
    210             215             220


Leu Cys Ala Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly
225             230             235             240


Thr Val Leu Ile Ile Lys Ser Leu Arg Ser Gly His Asp Pro Arg Ala
            245             250             255


Gln Gly Thr Leu
            260


<210> 2439
```

<211> 255
<212> PRT
<213> Homo sapiens

<400> 2439

Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Thr
1   5   10   15

Val Met Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala
                20   25   30

Ser Cys Gly Val Asn Leu Tyr Gln Phe Tyr Gly Pro Ser Gly Gln Tyr
            35   40   45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Glu Arg
        50   55   60

Lys Glu Thr Ala Trp Arg Trp Pro Glu Phe Ser Lys Phe Gly Gly Phe
65   70   75   80

Asp Pro Gln Gly Ala Leu Arg Asn Met Ala Val Ala Lys His Asn Leu
                85   90   95

Asn Ile Met Ile Lys Arg Tyr Asn Ser Thr Ala Ala Thr Asn Glu Val
            100   105   110

Pro Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro
        115   120   125

Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val Val Asn
        130   135   140

Ile Thr Trp Leu Ser Asn Gly Gln Ser Val Thr Glu Gly Val Ser Glu
145   150   155   160

Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr
                165   170   175

Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu
                180   185   190

His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp Glu Pro Glu Ile
        195   200   205

Pro Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly
        210   215   220

```
Leu Ser Val Gly Leu Met Gly Ile Val Val Gly Thr Val Phe Ile Ile
225             230             235             240
```

```
Gln Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
            245             250             255
```

<210> 2440
<211> 199
<212> PRT
<213> Homo sapiens

<400> 2440

```
Met Lys Ser Gly Leu Trp Tyr Phe Phe Leu Phe Cys Leu Arg Ile Lys
1               5               10              15
```

```
Val Leu Thr Gly Glu Ile Asn Gly Ser Ala Asn Tyr Glu Met Phe Ile
            20              25              30
```

```
Phe His Asn Gly Gly Val Gln Ile Leu Cys Lys Tyr Pro Asp Ile Val
        35              40              45
```

```
Gln Gln Phe Lys Met Gln Leu Leu Lys Gly Gly Gln Ile Leu Cys Asp
    50              55              60
```

```
Leu Thr Lys Thr Lys Gly Ser Gly Asn Thr Val Ser Ile Lys Ser Leu
65              70              75              80
```

```
Lys Phe Cys His Ser Gln Leu Ser Asn Asn Ser Val Ser Phe Phe Leu
            85              90              95
```

```
Tyr Asn Leu Asp His Ser His Ala Asn Tyr Tyr Phe Cys Asn Leu Ser
        100             105             110
```

```
Ile Phe Asp Pro Pro Pro Phe Lys Val Thr Leu Thr Gly Gly Tyr Leu
        115             120             125
```

```
His Ile Tyr Glu Ser Gln Leu Cys Cys Gln Leu Lys Phe Trp Leu Pro
    130             135             140
```

```
Ile Gly Cys Ala Ala Phe Val Val Val Cys Ile Leu Gly Cys Ile Leu
145             150             155             160
```

```
Ile Cys Trp Leu Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro
            165             170             175
```

```
Asn Gly Glu Tyr Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser
```

```
                180                    185                     190


Arg Leu Thr Asp Val Thr Leu
        195


<210>  2441
<211>  193
<212>  PRT
<213>  Homo sapiens


<400>  2441

Met Ala Ala Glu Pro Val Glu Asp Asn Cys Ile Asn Phe Val Ala Met
1               5                   10                  15


Lys Phe Ile Asp Asn Thr Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn
                20                  25                  30


Leu Glu Ser Asp Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile
            35                  40                  45


Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro
        50                  55                  60


Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg
65                  70                  75                  80


Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met
                85                  90                  95


Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys
            100                 105                 110


Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile
        115                 120                 125


Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly
    130                 135                 140


His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe
145                 150                 155                 160


Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys
                165                 170                 175


Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu
            180                 185                 190
```

751

Asp

<210>   2442
<211>   152
<212>   PRT
<213>   Homo sapiens

<400>   2442

Met Ser Arg Leu Pro Val Leu Leu Leu Gln Leu Leu Val Arg Pro
1   5   10   15

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Pro Leu Lys Thr Ser Trp
            20   25   30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
        35   40   45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln
    50   55   60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65   70   75   80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
            85   90   95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
            100   105   110

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
            115   120   125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
    130   135   140

Thr Thr Leu Ser Leu Ala Ile Phe
145   150

<210>   2443
<211>   1038
<212>   PRT
<213>   Homo sapiens

<400>   2443

Met Phe Pro Thr Glu Ser Ala Trp Leu Gly Lys Arg Gly Ala Asn Pro
1   5   10   15

```
Gly Pro Glu Ala Ala Val Arg Glu Thr Val Met Leu Leu Leu Cys Leu
        20                  25              30

Gly Val Pro Thr Gly Arg Pro Tyr Asn Val Asp Thr Glu Ser Ala Leu
        35                  40              45

Leu Tyr Gln Gly Pro His Asn Thr Leu Phe Gly Tyr Ser Val Val Leu
    50                  55              60

His Ser His Gly Ala Asn Arg Trp Leu Leu Val Gly Ala Pro Thr Ala
65              70              75              80

Asn Trp Leu Ala Asn Ala Ser Val Ile Asn Pro Gly Ala Ile Tyr Arg
                85              90              95

Cys Arg Ile Gly Lys Asn Pro Gly Gln Thr Cys Glu Gln Leu Gln Leu
            100             105             110

Gly Ser Pro Asn Gly Glu Pro Cys Gly Lys Thr Cys Leu Glu Glu Arg
            115             120             125

Asp Asn Gln Trp Leu Gly Val Thr Leu Ser Arg Gln Pro Gly Glu Asn
    130             135             140

Gly Ser Ile Val Thr Cys Gly His Arg Trp Lys Asn Ile Phe Tyr Ile
145             150             155             160

Lys Asn Glu Asn Lys Leu Pro Thr Gly Gly Cys Tyr Gly Val Pro Pro
            165             170             175

Asp Leu Arg Thr Glu Leu Ser Lys Arg Ile Ala Pro Cys Tyr Gln Asp
            180             185             190

Tyr Val Lys Lys Phe Gly Glu Asn Phe Ala Ser Cys Gln Ala Gly Ile
        195             200             205

Ser Ser Phe Tyr Thr Lys Asp Leu Ile Val Met Gly Ala Pro Gly Ser
    210             215             220

Ser Tyr Trp Thr Gly Ser Leu Phe Val Tyr Asn Ile Thr Thr Asn Lys
225             230             235             240

Tyr Lys Ala Phe Leu Asp Lys Gln Asn Gln Val Lys Phe Gly Ser Tyr
            245             250             255
```

753

```
Leu Gly Tyr Ser Val Gly Ala Gly His Phe Arg Ser Gln His Thr Thr
            260              265              270

Glu Val Val Gly Gly Ala Pro Gln His Glu Gln Ile Gly Lys Ala Tyr
        275              280              285

Ile Phe Ser Ile Asp Glu Lys Glu Leu Asn Ile Leu His Glu Met Lys
    290              295              300

Gly Lys Lys Leu Gly Ser Tyr Phe Gly Ala Ser Val Cys Ala Val Asp
305              310              315              320

Leu Asn Ala Asp Gly Phe Ser Asp Leu Leu Val Gly Ala Pro Met Gln
                325              330              335

Ser Thr Ile Arg Glu Glu Gly Arg Val Phe Val Tyr Ile Asn Ser Gly
            340              345              350

Ser Gly Ala Val Met Asn Ala Met Glu Thr Asn Leu Val Gly Ser Asp
        355              360              365

Lys Tyr Ala Ala Arg Phe Gly Glu Ser Ile Val Asn Leu Gly Asp Ile
    370              375              380

Asp Asn Asp Gly Phe Glu Asp Val Ala Ile Gly Ala Pro Gln Glu Asp
385              390              395              400

Asp Leu Gln Gly Ala Ile Tyr Ile Tyr Asn Gly Arg Ala Asp Gly Ile
                405              410              415

Ser Ser Thr Phe Ser Gln Arg Ile Glu Gly Leu Gln Ile Ser Lys Ser
            420              425              430

Leu Ser Met Phe Gly Gln Ser Ile Ser Gly Gln Ile Asp Ala Asp Asn
            435              440              445

Asn Gly Tyr Val Asp Val Ala Val Gly Ala Phe Arg Ser Asp Ser Ala
    450              455              460

Val Leu Leu Arg Thr Arg Pro Val Val Ile Val Asp Ala Ser Leu Ser
465              470              475              480

His Pro Glu Ser Val Asn Arg Thr Lys Phe Asp Cys Val Glu Asn Gly
                485              490              495
```

Trp Pro Ser Val Cys Ile Asp Leu Thr Leu Cys Phe Ser Tyr Lys Gly
            500   505   510

Lys Glu Val Pro Gly Tyr Ile Val Leu Phe Tyr Asn Met Ser Leu Asp
            515   520   525

Val Asn Arg Lys Ala Glu Ser Pro Pro Arg Phe Tyr Phe Ser Ser Asn
        530   535   540

Gly Thr Ser Asp Val Ile Thr Gly Ser Ile Gln Val Ser Ser Arg Glu
545   550   555   560

Ala Asn Cys Arg Thr His Gln Ala Phe Met Arg Lys Asp Val Arg Asp
            565   570   575

Ile Leu Thr Pro Ile Gln Ile Glu Ala Ala Tyr His Leu Gly Pro His
            580   585   590

Val Ile Ser Lys Arg Ser Thr Glu Glu Phe Pro Pro Leu Gln Pro Ile
        595   600   605

Leu Gln Gln Lys Lys Glu Lys Asp Ile Met Lys Lys Thr Ile Asn Phe
    610   615   620

Ala Arg Phe Cys Ala His Glu Asn Cys Ser Ala Asp Leu Gln Val Ser
625   630   635   640

Ala Lys Ile Gly Phe Leu Lys Pro His Glu Asn Lys Thr Tyr Leu Ala
            645   650   655

Val Gly Ser Met Lys Thr Leu Met Leu Asn Val Ser Leu Phe Asn Ala
            660   665   670

Gly Asp Asp Ala Tyr Glu Thr Thr Leu His Val Lys Leu Pro Val Gly
        675   680   685

Leu Tyr Phe Ile Lys Ile Leu Glu Leu Glu Glu Lys Gln Ile Asn Cys
    690   695   700

Glu Val Thr Asp Asn Ser Gly Val Val Gln Leu Asp Cys Ser Ile Gly
705   710   715   720

Tyr Ile Tyr Val Asp His Leu Ser Arg Ile Asp Ile Ser Phe Leu Leu
            725   730   735

Asp Val Ser Ser Leu Ser Arg Ala Glu Glu Asp Leu Ser Ile Thr Val

755

```
              740                      745                      750

      His Ala Thr Cys Glu Asn Glu Glu Glu Met Asp Asn Leu Lys His Ser
          755                  760              765

      Arg Val Thr Val Ala Ile Pro Leu Lys Tyr Glu Val Lys Leu Thr Val
          770                  775              780

      His Gly Phe Val Asn Pro Thr Ser Phe Val Tyr Gly Ser Asn Asp Glu
      785                  790              795                  800

      Asn Glu Pro Glu Thr Cys Met Val Glu Lys Met Asn Leu Thr Phe His
                  805              810                  815

      Val Ile Asn Thr Gly Asn Ser Met Ala Pro Asn Val Ser Val Glu Ile
              820              825                  830

      Met Val Pro Asn Ser Phe Ser Pro Gln Thr Asp Lys Leu Phe Asn Ile
              835              840                  845

      Leu Asp Val Gln Thr Thr Thr Gly Glu Cys His Phe Glu Asn Tyr Gln
          850                  855              860

      Arg Val Cys Ala Leu Glu Gln Gln Lys Ser Ala Met Gln Thr Leu Lys
      865                  870              875                  880

      Gly Ile Val Arg Phe Leu Ser Lys Thr Asp Lys Arg Leu Leu Tyr Cys
                  885              890                  895

      Ile Lys Ala Asp Pro His Cys Leu Asn Phe Leu Cys Asn Phe Gly Lys
              900              905                  910

      Met Glu Ser Gly Lys Glu Ala Ser Val His Ile Gln Leu Glu Gly Arg
              915              920                  925

      Pro Ser Ile Leu Glu Met Asp Glu Thr Ser Ala Leu Lys Phe Glu Ile
          930                  935              940

      Arg Ala Thr Gly Phe Pro Glu Pro Asn Pro Arg Val Ile Glu Leu Asn
      945                  950              955                  960

      Lys Asp Glu Asn Val Ala His Val Leu Leu Glu Gly Leu His His Gln
                  965              970                  975

      Arg Pro Lys Arg Tyr Phe Thr Ile Val Ile Ser Ser Ser Leu Leu
                  980              985                  990
```

```
Leu Gly Leu Ile Val Leu Leu Leu  Ile Ser Tyr Val Met  Trp Lys Ala
    995               1000              1005


Gly Phe  Phe Lys Arg Gln Tyr  Lys Ser Ile Leu Gln  Glu Glu Asn
    1010              1015              1020


Arg Arg  Asp Ser Trp Ser Tyr  Ile Asn Ser Lys Ser  Asn Asp Asp
    1025              1030              1035
```

```
<210>  2444
<211>  1152
<212>  PRT
<213>  Homo sapiens

<400>  2444
```

```
Met Ala Leu Arg Val Leu Leu Leu Thr Ala Leu Thr Leu Cys His Gly
1           5               10              15


Phe Asn Leu Asp Thr Glu Asn Ala Met Thr Phe Gln Glu Asn Ala Arg
        20              25              30


Gly Phe Gly Gln Ser Val Val Gln Leu Gln Gly Ser Arg Val Val Val
        35              40              45


Gly Ala Pro Gln Glu Ile Val Ala Ala Asn Gln Arg Gly Ser Leu Tyr
    50              55              60


Gln Cys Asp Tyr Ser Thr Gly Ser Cys Glu Pro Ile Arg Leu Gln Val
65              70              75              80


Pro Val Glu Ala Val Asn Met Ser Leu Gly Leu Ser Leu Ala Ala Thr
            85              90              95


Thr Ser Pro Pro Gln Leu Leu Ala Cys Gly Pro Thr Val His Gln Thr
        100             105             110


Cys Ser Glu Asn Thr Tyr Val Lys Gly Leu Cys Phe Leu Phe Gly Ser
        115             120             125


Asn Leu Arg Gln Gln Pro Gln Lys Phe Pro Glu Ala Leu Arg Gly Cys
    130             135             140


Pro Gln Glu Asp Ser Asp Ile Ala Phe Leu Ile Asp Gly Ser Gly Ser
145             150             155             160
```

```
Ile Ile Pro His Asp Phe Arg Arg Met Lys Glu Phe Val Ser Thr Val
            165                 170             175


Met Glu Gln Leu Lys Lys Ser Lys Thr Leu Phe Ser Leu Met Gln Tyr
            180                 185             190


Ser Glu Glu Phe Arg Ile His Phe Thr Phe Lys Glu Phe Gln Asn Asn
            195                 200             205


Pro Asn Pro Arg Ser Leu Val Lys Pro Ile Thr Gln Leu Leu Gly Arg
            210             215             220


Thr His Thr Ala Thr Gly Ile Arg Lys Val Val Arg Glu Leu Phe Asn
225             230             235             240


Ile Thr Asn Gly Ala Arg Lys Asn Ala Phe Lys Ile Leu Val Val Ile
            245                 250             255


Thr Asp Gly Glu Lys Phe Gly Asp Pro Leu Gly Tyr Glu Asp Val Ile
            260                 265             270


Pro Glu Ala Asp Arg Glu Gly Val Ile Arg Tyr Val Ile Gly Val Gly
            275             280             285


Asp Ala Phe Arg Ser Glu Lys Ser Arg Gln Glu Leu Asn Thr Ile Ala
    290             295             300


Ser Lys Pro Pro Arg Asp His Val Phe Gln Val Asn Asn Phe Glu Ala
305             310             315             320


Leu Lys Thr Ile Gln Asn Gln Leu Arg Glu Lys Ile Phe Ala Ile Glu
            325             330             335


Gly Thr Gln Thr Gly Ser Ser Ser Ser Phe Glu His Glu Met Ser Gln
            340             345             350


Glu Gly Phe Ser Ala Ala Ile Thr Ser Asn Gly Pro Leu Leu Ser Thr
            355             360             365


Val Gly Ser Tyr Asp Trp Ala Gly Gly Val Phe Leu Tyr Thr Ser Lys
    370             375             380


Glu Lys Ser Thr Phe Ile Asn Met Thr Arg Val Asp Ser Asp Met Asn
385             390             395             400


Asp Ala Tyr Leu Gly Tyr Ala Ala Ala Ile Ile Leu Arg Asn Arg Val
```

758

```
                    405                    410                    415

Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Ile Gly Leu Val
        420                    425                    430


Ala Met Phe Arg Gln Asn Thr Gly Met Trp Glu Ser Asn Ala Asn Val
        435                    440                    445


Lys Gly Thr Gln Ile Gly Ala Tyr Phe Gly Ala Ser Leu Cys Ser Val
    450                    455                    460


Asp Val Asp Ser Asn Gly Ser Thr Asp Leu Val Leu Ile Gly Ala Pro
465                    470                    475                    480


His Tyr Tyr Glu Gln Thr Arg Gly Gly Gln Val Ser Val Cys Pro Leu
            485                    490                    495


Pro Arg Gly Arg Ala Arg Trp Gln Cys Asp Ala Val Leu Tyr Gly Glu
        500                    505                    510


Gln Gly Gln Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu Gly
        515                    520                    525


Asp Val Asn Gly Asp Lys Leu Thr Asp Val Ala Ile Gly Ala Pro Gly
    530                    535                    540


Glu Glu Asp Asn Arg Gly Ala Val Tyr Leu Phe His Gly Thr Ser Gly
545                    550                    555                    560


Ser Gly Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Lys Leu
            565                    570                    575


Ser Pro Arg Leu Gln Tyr Phe Gly Gln Ser Leu Ser Gly Gly Gln Asp
        580                    585                    590


Leu Thr Met Asp Gly Leu Val Asp Leu Thr Val Gly Ala Gln Gly His
        595                    600                    605


Val Leu Leu Leu Arg Ser Gln Pro Val Leu Arg Val Lys Ala Ile Met
    610                    615                    620


Glu Phe Asn Pro Arg Glu Val Ala Arg Asn Val Phe Glu Cys Asn Asp
625                    630                    635                    640


Gln Val Val Lys Gly Lys Glu Ala Gly Glu Val Arg Val Cys Leu His
            645                    650                    655
```

```
Val Gln Lys Ser Thr Arg Asp Arg Leu Arg Glu Gly Gln Ile Gln Ser
            660             665             670

Val Val Thr Tyr Asp Leu Ala Leu Asp Ser Gly Arg Pro His Ser Arg
            675             680             685

Ala Val Phe Asn Glu Thr Lys Asn Ser Thr Arg Arg Gln Thr Gln Val
            690             695             700

Leu Gly Leu Thr Gln Thr Cys Glu Thr Leu Lys Leu Gln Leu Pro Asn
705             710             715             720

Cys Ile Glu Asp Pro Val Ser Pro Ile Val Leu Arg Leu Asn Phe Ser
                725             730             735

Leu Val Gly Thr Pro Leu Ser Ala Phe Gly Asn Leu Arg Pro Val Leu
            740             745             750

Ala Glu Asp Ala Gln Arg Leu Phe Thr Ala Leu Phe Pro Phe Glu Lys
            755             760             765

Asn Cys Gly Asn Asp Asn Ile Cys Gln Asp Asp Leu Ser Ile Thr Phe
            770             775             780

Ser Phe Met Ser Leu Asp Cys Leu Val Val Gly Gly Pro Arg Glu Phe
785             790             795             800

Asn Val Thr Val Thr Val Arg Asn Asp Gly Glu Asp Ser Tyr Arg Thr
                805             810             815

Gln Val Thr Phe Phe Phe Pro Leu Asp Leu Ser Tyr Arg Lys Val Ser
            820             825             830

Thr Leu Gln Asn Gln Arg Ser Gln Arg Ser Trp Arg Leu Ala Cys Glu
            835             840             845

Ser Ala Ser Ser Thr Glu Val Ser Gly Ala Leu Lys Ser Thr Ser Cys
850             855             860

Ser Ile Asn His Pro Ile Phe Pro Glu Asn Ser Glu Val Thr Phe Asn
865             870             875             880

Ile Thr Phe Asp Val Asp Ser Lys Ala Ser Leu Gly Asn Lys Leu Leu
                885             890             895
```

Leu Lys Ala Asn Val Thr Ser Glu Asn Asn Met Pro Arg Thr Asn Lys
        900   905   910

Thr Glu Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Met Val
        915   920   925

Val Thr Ser His Gly Val Ser Thr Lys Tyr Leu Asn Phe Thr Ala Ser
    930   935   940

Glu Asn Thr Ser Arg Val Met Gln His Gln Tyr Gln Val Ser Asn Leu
945   950   955   960

Gly Gln Arg Ser Pro Pro Ile Ser Leu Val Phe Leu Val Pro Val Arg
                965   970   975

Leu Asn Gln Thr Val Ile Trp Asp Arg Pro Gln Val Thr Phe Ser Glu
        980   985   990

Asn Leu Ser Ser Thr Cys His Thr Lys Glu Arg Leu Pro Ser His Ser
        995   1000   1005

Asp Phe Leu Ala Glu Leu Arg Lys Ala Pro Val Val Asn Cys Ser
    1010   1015   1020

Ile Ala Val Cys Gln Arg Ile Gln Cys Asp Ile Pro Phe Phe Gly
    1025   1030   1035

Ile Gln Glu Glu Phe Asn Ala Thr Leu Lys Gly Asn Leu Ser Phe
    1040   1045   1050

Asp Trp Tyr Ile Lys Thr Ser His Asn His Leu Leu Ile Val Ser
    1055   1060   1065

Thr Ala Glu Ile Leu Phe Asn Asp Ser Val Phe Thr Leu Leu Pro
    1070   1075   1080

Gly Gln Gly Ala Phe Val Arg Ser Gln Thr Glu Thr Lys Val Glu
    1085   1090   1095

Pro Phe Glu Val Pro Asn Pro Leu Pro Leu Ile Val Gly Ser Ser
    1100   1105   1110

Val Gly Gly Leu Leu Leu Leu Ala Leu Ile Thr Ala Ala Leu Tyr
    1115   1120   1125

761

Lys Leu Gly Phe Phe Lys Arg Gln Tyr Lys Asp Met Met Ser Glu
    1130   1135   1140

Gly Gly Pro Pro Gly Ala Glu Pro Gln
    1145   1150

<210> 2445.
<211> 798
<212> PRT
<213> Homo sapiens

<400> 2445

Met Val Ala Leu Pro Met Val Leu Val Leu Leu Leu Val Leu Ser Arg
1   5   10   15

Gly Glu Ser Glu Leu Asp Ala Lys Ile Pro Ser Thr Gly Asp Ala Thr
            20   25   30

Glu Trp Arg Asn Pro His Leu Ser Met Leu Gly Ser Cys Gln Pro Ala
        35   40   45

Pro Ser Cys Gln Lys Cys Ile Leu Ser His Pro Ser Cys Ala Trp Cys
    50   55   60

Lys Gln Leu Asn Phe Thr Ala Ser Gly Glu Ala Glu Ala Arg Arg Cys
65   70   75   80

Ala Arg Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu
            85   90   95

Glu Glu Pro Arg Gly Gln Gln Glu Val Leu Gln Asp Gln Pro Leu Ser
            100   105   110

Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val
        115   120   125

Arg Val Thr Leu Arg Pro Gly Glu Pro Gln Gln Leu Gln Val Arg Phe
    130   135   140

Leu Arg Ala Glu Gly Tyr Pro Val Asp Leu Tyr Tyr Leu Met Asp Leu
145   150   155   160

Ser Tyr Ser Met Lys Asp Asp Leu Glu Arg Val Arg Gln Leu Gly His
            165   170   175

Ala Leu Leu Val Arg Leu Gln Glu Val Thr His Ser Val Arg Ile Gly
            180   185   190

                            762

Phe Gly Ser Phe Val Asp Lys Thr Val Leu Pro Phe Val Ser Thr Val
        195   200   205

Pro Ser Lys Leu Arg His Pro Cys Pro Thr Arg Leu Glu Arg Cys Gln
    210   215   220

Ser Pro Phe Ser Phe His His Val Leu Ser Leu Thr Gly Asp Ala Gln
225   230   235   240

Ala Phe Glu Arg Glu Val Gly Arg Gln Ser Val Ser Gly Asn Leu Asp
                245   250   255

Ser Pro Glu Gly Gly Phe Asp Ala Ile Leu Gln Ala Ala Leu Cys Gln
            260   265   270

Glu Gln Ile Gly Trp Arg Asn Val Ser Arg Leu Leu Val Phe Thr Ser
        275   280   285

Asp Asp Thr Phe His Thr Ala Gly Asp Gly Lys Leu Gly Gly Ile Phe
    290   295   300

Met Pro Ser Asp Gly His Cys His Leu Asp Ser Asn Gly Leu Tyr Ser
305   310   315   320

Arg Ser Thr Glu Phe Asp Tyr Pro Ser Val Gly Gln Val Ala Gln Ala
            325   330   335

Leu Ser Ala Ala Asn Ile Gln Pro Ile Phe Ala Val Thr Ser Ala Ala
        340   345   350

Leu Pro Val Tyr Gln Glu Leu Ser Lys Leu Ile Pro Lys Ser Ala Val
        355   360   365

Gly Glu Leu Ser Glu Asp Ser Ser Asn Val Val Gln Leu Ile Met Asp
    370   375   380

Ala Tyr Asn Ser Leu Ser Ser Thr Val Thr Leu Glu His Ser Ser Leu
385   390   395   400

Pro Pro Gly Val His Ile Ser Tyr Glu Ser Gln Cys Glu Gly Pro Glu
            405   410   415

Lys Arg Glu Gly Lys Ala Glu Asp Arg Gly Gln Cys Asn His Val Arg
        420   425   430

763

Ile Asn Gln Thr Val Thr Phe Trp Val Ser Leu Gln Ala Thr His Cys
        435   440   445

Leu Pro Glu Pro His Leu Leu Arg Leu Arg Ala Leu Gly Phe Ser Glu
        450   455   460

Glu Leu Ile Val Glu Leu His Thr Leu Cys Asp Cys Asn Cys Ser Asp
465   470   475   480

Thr Gln Pro Gln Ala Pro His Cys Ser Asp Gly Gln Gly His Leu Gln
                485   490   495

Cys Gly Val Cys Ser Cys Ala Pro Gly Arg Leu Gly Arg Leu Cys Glu
            500   505   510

Cys Ser Val Ala Glu Leu Ser Ser Pro Asp Leu Glu Ser Gly Cys Arg
        515   520   525

Ala Pro Asn Gly Thr Gly Pro Leu Cys Ser Gly Lys Gly His Cys Gln
    530   535   540

Cys Gly Arg Cys Ser Cys Ser Gly Gln Ser Ser Gly His Leu Cys Glu
545   550   555   560

Cys Asp Asp Ala Ser Cys Glu Arg His Glu Gly Ile Leu Cys Gly Gly
                565   570   575

Phe Gly Arg Cys Gln Cys Gly Val Cys His Cys His Ala Asn Arg Thr
        580   585   590

Gly Arg Ala Cys Glu Cys Ser Gly Asp Met Asp Ser Cys Ile Ser Pro
        595   600   605

Glu Gly Gly Leu Cys Ser Gly His Gly Arg Cys Lys Cys Asn Arg Cys
    610   615   620

Gln Cys Leu Asp Gly Tyr Tyr Gly Ala Leu Cys Asp Gln Cys Pro Gly
625   630   635   640

Cys Lys Thr Pro Cys Glu Arg His Arg Asp Cys Ala Glu Cys Gly Ala
            645   650   655

Phe Arg Thr Gly Pro Leu Ala Thr Asn Cys Ser Thr Ala Cys Ala His
        660   665   670

Thr Asn Val Thr Leu Ala Leu Ala Pro Ile Leu Asp Asp Gly Trp Cys
        675   680   685

Lys Glu Arg Thr Leu Asp Asn Gln Leu Phe Phe Phe Leu Val Glu Asp
        690   695   700

Asp Ala Arg Gly Thr Val Val Leu Arg Val Arg Pro Gln Glu Lys Gly
705   710   715   720

Ala Asp His Thr Gln Ala Ile Val Leu Gly Cys Val Gly Gly Ile Val
            725   730   735

Ala Val Gly Leu Gly Leu Val Leu Ala Tyr Arg Leu Ser Val Glu Ile
            740   745   750

Tyr Asp Arg Arg Glu Tyr Ser Arg Phe Glu Lys Glu Gln Gln Gln Leu
        755   760   765

Asn Trp Lys Gln Asp Ser Asn Pro Leu Tyr Lys Ser Ala Ile Thr Thr
    770   775   780

Thr Ile Asn Pro Arg Phe Gln Glu Ala Asp Ser Pro Thr Leu
785   790   795

<210>   2446
<211>   345
<212>   PRT
<213>   Homo sapiens

<400>   2446

Met Gln Arg Leu Val Ala Trp Asp Pro Ala Cys Leu Pro Leu Pro Pro
1   5   10   15

Pro Pro Pro Ala Phe Lys Ser Met Glu Val Ala Asn Phe Tyr Tyr Glu
            20   25   30

Ala Asp Cys Leu Ala Ala Ala Tyr Gly Gly Lys Ala Ala Pro Ala Ala
            35   40   45

Pro Pro Ala Ala Arg Pro Gly Pro Arg Pro Pro Ala Gly Glu Leu Gly
        50   55   60

Ser Ile Gly Asp His Glu Arg Ala Ile Asp Phe Ser Pro Tyr Leu Glu
65   70   75   80

Pro Leu Gly Ala Pro Gln Ala Pro Ala Pro Ala Thr Ala Thr Asp Thr
                85   90   95

765

Phe Glu Ala Ala Pro Pro Ala Pro Ala Pro Ala Ser Ser Gly
            100   105   110

Gln His His Asp Phe Leu Ser Asp Leu Phe Ser Asp Asp Tyr Gly Gly
            115   120   125

Lys Asn Cys Lys Lys Pro Ala Glu Tyr Gly Tyr Val Ser Leu Gly Arg
        130   135   140

Leu Gly Ala Ala Lys Gly Ala Leu His Pro Gly Cys Phe Ala Pro Leu
145   150   155   160

His Pro Pro Pro Pro Pro Pro Pro Pro Ala Glu Leu Lys Ala Glu
            165   170   175

Pro Gly Phe Glu Pro Ala Asp Cys Lys Arg Lys Glu Glu Ala Gly Ala
            180   185   190

Pro Gly Gly Gly Ala Gly Met Ala Ala Gly Phe Pro Tyr Ala Leu Arg
            195   200   205

Ala Tyr Leu Gly Tyr Gln Ala Val Pro Ser Gly Ser Ser Gly Ser Leu
        210   215   220

Ser Thr Ser Ser Ser Ser Ser Pro Pro Gly Thr Pro Ser Pro Ala Asp
225   230   235   240

Ala Lys Ala Pro Pro Thr Ala Cys Tyr Ala Gly Ala Ala Pro Ala Pro
            245   250   255

Ser Gln Val Lys Ser Lys Ala Lys Lys Thr Val Asp Lys His Ser Asp
            260   265   270

Glu Tyr Lys Ile Arg Arg Glu Arg Asn Asn Ile Ala Val Arg Lys Ser
        275   280   285

Arg Asp Lys Ala Lys Met Arg Asn Leu Glu Thr Gln His Lys Val Leu
        290   295   300

Glu Leu Thr Ala Glu Asn Glu Arg Leu Gln Lys Lys Val Glu Gln Leu
305   310   315   320

Ser Arg Glu Leu Ser Thr Leu Arg Asn Leu Phe Lys Gln Leu Pro Glu
            325   330   335

```
Pro Leu Leu Ala Ser Ser Gly His Cys
            340                 345


<210>   2447
<211>   373
<212>   PRT
<213>   Homo sapiens


<400>   2447

Met Ser Pro Cys Pro Pro Gln Gln Ser Arg Asn Arg Val Ile Gln Leu
1               5                   10                  15


Ser Thr Ser Glu Leu Gly Glu Met Glu Leu Thr Trp Gln Glu Ile Met
            20                  25                  30


Ser Ile Thr Glu Leu Gln Gly Leu Asn Ala Pro Ser Glu Pro Ser Phe
            35                  40                  45


Glu Pro Gln Ala Pro Ala Pro Tyr Leu Gly Pro Pro Pro Pro Thr Thr
    50                  55                  60


Tyr Cys Pro Cys Ser Ile His Pro Asp Ser Gly Phe Pro Leu Pro Pro
65                  70                  75                  80


Pro Pro Tyr Glu Leu Pro Ala Ser Thr Ser His Val Pro Asp Pro Pro
            85                  90                  95


Tyr Ser Tyr Gly Asn Met Ala Ile Pro Val Ser Lys Pro Leu Ser Leu
            100                 105                 110


Ser Gly Leu Leu Ser Glu Pro Leu Gln Asp Pro Leu Ala Leu Leu Asp
            115                 120                 125


Ile Gly Leu Pro Ala Gly Pro Pro Lys Pro Gln Glu Asp Pro Glu Ser
    130                 135                 140


Asp Ser Gly Leu Ser Leu Asn Tyr Ser Asp Ala Glu Ser Leu Glu Leu
145                 150                 155                 160


Glu Gly Thr Glu Ala Gly Arg Arg Arg Ser Glu Tyr Val Glu Met Tyr
                165                 170                 175


Pro Val Glu Tyr Pro Tyr Ser Leu Met Pro Asn Ser Leu Ala His Ser
            180                 185                 190


Asn Tyr Thr Leu Pro Ala Ala Glu Thr Pro Leu Ala Leu Glu Pro Ser
```

767

            195   200   205

    Ser Gly Pro Val Arg Ala Lys Pro Thr Ala Arg Gly Glu Ala Gly Ser
        210   215   220

    Arg Asp Glu Arg Arg Ala Leu Ala Met Lys Ile Pro Phe Pro Thr Asp
    225   230   235   240

    Lys Ile Val Asn Leu Pro Val Asp Asp Phe Asn Glu Leu Leu Ala Arg
                245   250   255

    Tyr Pro Leu Thr Glu Ser Gln Leu Ala Leu Val Arg Asp Ile Arg Arg
                260   265   270

    Arg Gly Lys Asn Lys Val Ala Ala Gln Asn Cys Arg Lys Arg Lys Leu
                275   280   285

    Glu Thr Ile Val Gln Leu Glu Arg Glu Leu Glu Arg Leu Thr Asn Glu
        290   295   300

    Arg Glu Arg Leu Leu Arg Ala Arg Gly Glu Ala Asp Arg Thr Leu Glu
    305   310   315   320

    Val Met Arg Gln Gln Leu Thr Glu Leu Tyr Arg Asp Ile Phe Gln His
                325   330   335

    Leu Arg Asp Glu Ser Gly Asn Ser Tyr Ser Pro Glu Glu Tyr Ala Leu
                340   345   350

    Gln Gln Ala Ala Asp Gly Thr Ile Phe Leu Val Pro Arg Gly Thr Lys
                355   360   365

    Met Glu Ala Thr Asp
        370

    <210> 2448
    <211> 288
    <212> PRT
    <213> Homo sapiens

    <400> 2448

    Met Gln Ile Pro Gln Ala Pro Trp Pro Val Val Trp Ala Val Leu Gln
    1   5   10   15

    Leu Gly Trp Arg Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp
                20   25   30

```
Asn Pro Pro Thr Phe Phe Pro Ala Leu Leu Val Val Thr Glu Gly Asp
        35              40              45


Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val
    50              55              60


Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala
65              70              75              80


Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg
            85              90              95


Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg
            100             105             110


Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu
        115             120             125


Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val
    130             135             140


Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro
145             150             155             160


Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly
            165             170             175


Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys
            180             185             190


Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro
        195             200             205


Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly
    210             215             220


Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro
225             230             235             240


Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly
            245             250             255


Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg
            260             265             270
```

Ser Ala Gln Pro Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu
        275   280   285

<210> 2449
<211> 101
<212> PRT
<213> Homo sapiens

<400> 2449

Met Ser Ser Ala Ala Gly Phe Cys Ala Ser Arg Pro Gly Leu Leu Phe
1   5   10   15

Leu Gly Leu Leu Leu Leu Pro Leu Val Val Ala Phe Ala Ser Ala Glu
            20   25   30

Ala Glu Glu Asp Gly Asp Leu Gln Cys Leu Cys Val Lys Thr Thr Ser
        35   40   45

Gln Val Arg Pro Arg His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly
    50   55   60

Pro His Cys Pro Thr Ala Gln Leu Ile Ala Thr Leu Lys Asn Gly Arg
65   70   75   80

Lys Ile Cys Leu Asp Leu Gln Ala Pro Leu Tyr Lys Lys Ile Ile Lys
                85   90   95

Lys Leu Leu Glu Ser
            100

<210> 2450
<211> 706
<212> PRT
<213> Homo sapiens

<400> 2450

Met Ser Pro Phe Leu Arg Ile Gly Leu Ser Asn Phe Asp Cys Gly Ser
1   5   10   15

Cys Gln Ser Cys Gln Gly Glu Ala Val Asn Pro Tyr Cys Ala Val Leu
            20   25   30

Val Lys Glu Tyr Val Glu Ser Glu Asn Gly Gln Met Tyr Ile Gln Lys
        35   40   45

Lys Pro Thr Met Tyr Pro Pro Trp Asp Ser Thr Phe Asp Ala His Ile
    50   55   60

Asn Lys Gly Arg Val Met Gln Ile Ile Val Lys Gly Lys Asn Val Asp
65   70   75   80

Leu Ile Ser Glu Thr Thr Val Glu Leu Tyr Ser Leu Ala Glu Arg Cys
            85   90   95

Arg Lys Asn Asn Gly Lys Thr Glu Ile Trp Leu Glu Leu Lys Pro Gln
            100   105   110

Gly Arg Met Leu Met Asn Ala Arg Tyr Phe Leu Glu Met Ser Asp Thr
        115   120   125

Lys Asp Met Asn Glu Phe Glu Thr Glu Gly Phe Phe Ala Leu His Gln
    130   135   140

Arg Arg Gly Ala Ile Lys Gln Ala Lys Val His His Val Lys Cys His
145   150   155   160

Glu Phe Thr Ala Thr Phe Phe Pro Gln Pro Thr Phe Cys Ser Val Cys
            165   170   175

His Glu Phe Val Trp Gly Leu Asn Lys Gln Gly Tyr Gln Cys Arg Gln
            180   185   190

Cys Asn Ala Ala Ile His Lys Lys Cys Ile Asp Lys Val Ile Ala Lys
        195   200   205

Cys Thr Gly Ser Ala Ile Asn Ser Arg Glu Thr Met Phe His Lys Glu
    210   215   220

Arg Phe Lys Ile Asp Met Pro His Arg Phe Lys Val Tyr Asn Tyr Lys
225   230   235   240

Ser Pro Thr Phe Cys Glu His Cys Gly Thr Leu Leu Trp Gly Leu Ala
            245   250   255

Arg Gln Gly Leu Lys Cys Asp Ala Cys Gly Met Asn Val His His Arg
        260   265   270

Cys Gln Thr Lys Val Ala Asn Leu Cys Gly Ile Asn Gln Lys Leu Met
    275   280   285

Ala Glu Ala Leu Ala Met Ile Glu Ser Thr Gln Gln Ala Arg Cys Leu
    290   295   300

```
Arg Asp Thr Glu Gln Ile Phe Arg Glu Gly Pro Val Glu Ile Gly Leu
305             310             315             320


Pro Cys Ser Ile Lys Asn Glu Ala Arg Pro Pro Cys Leu Pro Thr Pro
                325             330             335


Gly Lys Arg Glu Pro Gln Gly Ile Ser Trp Glu Ser Pro Leu Asp Glu
            340             345             350


Val Asp Lys Met Cys His Leu Pro Glu Pro Glu Leu Asn Lys Glu Arg
            355             360             365


Pro Ser Leu Gln Ile Lys Leu Lys Ile Glu Asp Phe Ile Leu His Lys
    370             375             380


Met Leu Gly Lys Gly Ser Phe Gly Lys Val Phe Leu Ala Glu Phe Lys
385             390             395             400


Lys Thr Asn Gln Phe Phe Ala Ile Lys Ala Leu Lys Lys Asp Val Val
            405             410             415


Leu Met Asp Asp Asp Val Glu Cys Thr Met Val Glu Lys Arg Val Leu
            420             425             430


Ser Leu Ala Trp Glu His Pro Phe Leu Thr His Met Phe Cys Thr Phe
    435             440             445


Gln Thr Lys Glu Asn Leu Phe Phe Val Met Glu Tyr Leu Asn Gly Gly
    450             455             460


Asp Leu Met Tyr His Ile Gln Ser Cys His Lys Phe Asp Leu Ser Arg
465             470             475             480


Ala Thr Phe Tyr Ala Ala Glu Ile Ile Leu Gly Leu Gln Phe Leu His
            485             490             495


Ser Lys Gly Ile Val Tyr Arg Asp Leu Lys Leu Asp Asn Ile Leu Leu
            500             505             510


Asp Lys Asp Gly His Ile Lys Ile Ala Asp Phe Gly Met Cys Lys Glu
    515             520             525


Asn Met Leu Gly Asp Ala Lys Thr Asn Thr Phe Cys Gly Thr Pro Asp
    530             535             540


Tyr Ile Ala Pro Glu Ile Leu Leu Gly Gln Lys Tyr Asn His Ser Val
```

```
545                     550                    555                    560
```

```
Asp Trp Trp Ser Phe Gly Val Leu Leu Tyr Glu Met Leu Ile Gly Gln
            565                    570                    575
```

```
Ser Pro Phe His Gly Gln Asp Glu Glu Glu Leu Phe His Ser Ile Arg
            580                    585                    590
```

```
Met Asp Asn Pro Phe Tyr Pro Arg Trp Leu Glu Lys Glu Ala Lys Asp
            595                    600                    605
```

```
Leu Leu Val Lys Leu Phe Val Arg Glu Pro Glu Lys Arg Leu Gly Val
    610                    615                    620
```

```
Arg Gly Asp Ile Arg Gln His Pro Leu Phe Arg Glu Ile Asn Trp Glu
625                    630                    635                    640
```

```
Glu Leu Glu Arg Lys Glu Ile Asp Pro Pro Phe Arg Pro Lys Val Lys
            645                    650                    655
```

```
Ser Pro Phe Asp Cys Ser Asn Phe Asp Lys Glu Phe Leu Asn Glu Lys
            660                    665                    670
```

```
Pro Arg Leu Ser Phe Ala Asp Arg Ala Leu Ile Asn Ser Met Asp Gln
            675                    680                    685
```

```
Asn Met Phe Arg Asn Phe Ser Phe Met Asn Pro Gly Met Glu Arg Leu
            690                    695                    700
```

```
Ile Ser
705
```

```
<210>  2451
<211>  798
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2451
```

```
Met Ala Trp Asp Met Cys Asn Gln Asp Ser Glu Ser Val Trp Ser Asp
1               5                   10                     15
```

```
Ile Glu Cys Ala Ala Leu Val Gly Glu Asp Gln Pro Leu Cys Pro Asp
            20                     25                     30
```

```
Leu Pro Glu Leu Asp Leu Ser Glu Leu Asp Val Asn Asp Leu Asp Thr
            35                     40                     45
```

```
Asp Ser Phe Leu Gly Gly Leu Lys Trp Cys Ser Asp Gln Ser Glu Ile
    50              55              60

Ile Ser Asn Gln Tyr Asn Asn Glu Pro Ser Asn Ile Phe Glu Lys Ile
65              70              75              80

Asp Glu Glu Asn Glu Ala Asn Leu Leu Ala Val Leu Thr Glu Thr Leu
                85              90              95

Asp Ser Leu Pro Val Asp Glu Asp Gly Leu Pro Ser Phe Asp Ala Leu
            100             105             110

Thr Asp Gly Asp Val Thr Thr Asp Asn Glu Ala Ser Pro Ser Ser Met
        115             120             125

Pro Asp Gly Thr Pro Pro Gln Glu Ala Glu Glu Pro Ser Leu Leu
    130             135             140

Lys Lys Leu Leu Leu Ala Pro Ala Asn Thr Gln Leu Ser Tyr Asn Glu
145             150             155             160

Cys Ser Gly Leu Ser Thr Gln Asn His Ala Asn His Asn His Arg Ile
            165             170             175

Arg Thr Asn Pro Ala Ile Val Lys Thr Glu Asn Ser Trp Ser Asn Lys
        180             185             190

Ala Lys Ser Ile Cys Gln Gln Gln Lys Pro Gln Arg Arg Pro Cys Ser
    195             200             205

Glu Leu Leu Lys Tyr Leu Thr Thr Asn Asp Asp Pro Pro His Thr Lys
    210             215             220

Pro Thr Glu Asn Arg Asn Ser Ser Arg Asp Lys Cys Thr Ser Lys Lys
225             230             235             240

Lys Ser His Thr Gln Ser Gln Ser Gln His Leu Gln Ala Lys Pro Thr
            245             250             255

Thr Leu Ser Leu Pro Leu Thr Pro Glu Ser Pro Asn Asp Pro Lys Gly
        260             265             270

Ser Pro Phe Glu Asn Lys Thr Ile Glu Arg Thr Leu Ser Val Glu Leu
    275             280             285
```

Ser Gly Thr Ala Gly Leu Thr Pro Pro Thr Thr Pro Pro His Lys Ala
    290   295   300

Asn Gln Asp Asn Pro Phe Arg Ala Ser Pro Lys Leu Lys. Ser Ser Cys
305   310   315   320

Lys Thr Val Val Pro Pro Pro Ser Lys Lys Pro Arg Tyr Ser Glu Ser
            325   330   335

Ser Gly Thr Gln Gly Asn Asn Ser Thr Lys Lys Gly Pro Glu Gln Ser
            340   345   350

Glu Leu Tyr Ala Gln Leu Ser Lys Ser Ser Val Leu Thr Gly Gly His
            355   360   365

Glu Glu Arg Lys Thr Lys Arg Pro Ser Leu Arg Leu Phe Gly Asp His
    370   375   380

Asp Tyr Cys Gln Ser Ile Asn Ser Lys Thr Glu Ile Leu Ile Asn Ile
385   390   395   400

Ser Gln Glu Leu Gln Asp Ser Arg Gln Leu Glu Asn Lys Asp Val Ser
            405   410   415

Ser Asp Trp Gln Gly Gln Ile Cys Ser Ser Thr Asp Ser Asp Gln Cys
            420   425   430

Tyr Leu Arg Glu Thr Leu Glu Ala Ser Lys Gln Val Ser Pro Cys Ser
            435   440   445

Thr Arg Lys Gln Leu Gln Asp Gln Glu Ile Arg Ala Glu Leu Asn Lys
    450   455   460

His Phe Gly His Pro Ser Gln Ala Val Phe Asp Asp Glu Ala Asp Lys
465   470   475   480

Thr Gly Glu Leu Arg Asp Ser Asp Phe Ser Asn Glu Gln Phe Ser Lys
            485   490   495

Leu Pro Met Phe Ile Asn Ser Gly Leu Ala Met Asp Gly Leu Phe Asp
            500   505   510

Asp Ser Glu Asp Glu Ser Asp Lys Leu Ser Tyr Pro Trp Asp Gly Thr
    515   520   525

Gln Ser Tyr Ser Leu Phe Asn Val Ser Pro Ser Cys Ser Ser Phe Asn

```
           530                    535                    540
```

Ser Pro Cys Arg Asp Ser Val Ser Pro Pro Lys Ser Leu Phe Ser Gln
545   550   555   560

Arg Pro Gln Arg Met Arg Ser Arg Ser Arg Ser Phe Ser Arg His Arg
                565   570   575

Ser Cys Ser Arg Ser Pro Tyr Ser Arg Ser Arg Ser Arg Ser Pro Gly
                580   585   590

Ser Arg Ser Ser Ser Arg Ser Cys Tyr Tyr Tyr Glu Ser Ser His Tyr
          595   600   605

Arg His Arg Thr His Arg Asn Ser Pro Leu Tyr Val Arg Ser Arg Ser
    610   615   620

Arg Ser Pro Tyr Ser Arg Arg Pro Arg Tyr Asp Ser Tyr Glu Glu Tyr
625   630   635   640

Gln His Glu Arg Leu Lys Arg Glu Glu Tyr Arg Arg Glu Tyr Glu Lys
                645   650   655

Arg Glu Ser Glu Arg Ala Lys Gln Arg Glu Arg Gln Arg Gln Lys Ala
          660   665   670

Ile Glu Glu Arg Arg Val Ile Tyr Val Gly Lys Ile Arg Pro Asp Thr
    675   680   685

Thr Arg Thr Glu Leu Arg Asp Arg Phe Glu Val Phe Gly Glu Ile Glu
    690   695   700

Glu Cys Thr Val Asn Leu Arg Asp Asp Gly Asp Ser Tyr Gly Phe Ile
705   710   715   720

Thr Tyr Arg Tyr Thr Cys Asp Ala Phe Ala Ala Leu Glu Asn Gly Tyr
                725   730   735

Thr Leu Arg Arg Ser Asn Glu Thr Asp Phe Glu Leu Tyr Phe Cys Gly
                740   745   750

Arg Lys Gln Phe Phe Lys Ser Asn Tyr Ala Asp Leu Asp Ser Asn Ser
          755   760   765

Asp Asp Phe Asp Pro Ala Ser Thr Lys Ser Lys Tyr Asp Ser Leu Asp
770   775   780

```
Phe Asp Ser Leu Leu Lys Glu Ala Gln Arg Ser Leu Arg Arg
785             790             795
```

```
<210>  2452
<211>  1043
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2452
```

```
Met Ala Ala Ser Phe Pro Pro Thr Leu Gly Leu Ser Ser Ala Pro Asp
1             5             10             15
```

```
Glu Ile Gln His Pro His Ile Lys Phe Ser Glu Trp Lys Phe Lys Leu
            20             25             30
```

```
Phe Arg Val Arg Ser Phe Glu Lys Thr Pro Glu Glu Ala Gln Lys Glu
        35             40             45
```

```
Lys Lys Asp Ser Phe Glu Gly Lys Pro Ser Leu Glu Gln Ser Pro Ala
    50             55             60
```

```
Val Leu Asp Lys Ala Asp Gly Gln Lys Pro Val Pro Thr Gln Pro Leu
65             70             75             80
```

```
Leu Lys Ala His Pro Lys Phe Ser Lys Lys Phe His Asp Asn Glu Lys
            85             90             95
```

```
Ala Arg Gly Lys Ala Ile His Gln Ala Asn Leu Arg His Leu Cys Arg
            100            105            110
```

```
Ile Cys Gly Asn Ser Phe Arg Ala Asp Glu His Asn Arg Arg Tyr Pro
        115            120            125
```

```
Val His Gly Pro Val Asp Gly Lys Thr Leu Gly Leu Leu Arg Lys Lys
    130            135            140
```

```
Glu Lys Arg Ala Thr Ser Trp Pro Asp Leu Ile Ala Lys Val Phe Arg
145            150            155            160
```

```
Ile Asp Val Lys Ala Asp Val Asp Ser Ile His Pro Thr Glu Phe Cys
            165            170            175
```

```
His Asn Cys Trp Ser Ile Met His Arg Lys Phe Ser Ser Ala Pro Cys
            180            185            190
```

Glu Val Tyr Phe Pro Arg Asn Val Thr Met Glu Trp His Pro His Thr
        195   200   205

Pro Ser Cys Asp Ile Cys Asn Thr Ala Arg Arg Gly Leu Lys Arg Lys
    210   215   220

Ser Leu Gln Pro Asn Leu Gln Leu Ser Lys Lys Leu Lys Thr Val Leu
225   230   235   240

Asp Gln Ala Arg Gln Ala Arg Gln Arg Lys Arg Arg Ala Gln Ala Arg
            245   250   255

Ile Ser Ser Lys Asp Val Met Lys Lys Ile Ala Asn Cys Ser Lys Ile
        260   265   270

His Leu Ser Thr Lys Leu Leu Ala Val Asp Phe Pro Glu His Phe Val
        275   280   285

Lys Ser Ile Ser Cys Gln Ile Cys Glu His Ile Leu Ala Asp Pro Val
    290   295   300

Glu Thr Asn Cys Lys His Val Phe Cys Arg Val Cys Ile Leu Arg Cys
305   310   315   320

Leu Lys Val Met Gly Ser Tyr Cys Pro Ser Cys Arg Tyr Pro Cys Phe
            325   330   335

Pro Thr Asp Leu Glu Ser Pro Val Lys Ser Phe Leu Ser Val Leu Asn
        340   345   350

Ser Leu Met Val Lys Cys Pro Ala Lys Glu Cys Asn Glu Glu Val Ser
        355   360   365

Leu Glu Lys Tyr Asn His His Ile Ser Ser His Lys Glu Ser Lys Glu
        370   375   380

Ile Phe Val His Ile Asn Lys Gly Gly Arg Pro Arg Gln His Leu Leu
385   390   395   400

Ser Leu Thr Arg Arg Ala Gln Lys His Arg Leu Arg Glu Leu Lys Leu
            405   410   415

Gln Val Lys Ala Phe Ala Asp Lys Glu Glu Gly Gly Asp Val Lys Ser
            420   425   430

Val Cys Met Thr Leu Phe Leu Leu Ala Leu Arg Ala Arg Asn Glu His

```
        435              440                445
```

Arg Gln Ala Asp Glu Leu Glu Ala Ile Met Gln Gly Lys Gly Ser Gly
    450   455   460

Leu Gln Pro Ala Val Cys Leu Ala Ile Arg Val Asn Thr Phe Leu Ser
465   470   475   480

Cys Ser Gln Tyr His Lys Met Tyr Arg Thr Val Lys Ala Ile Thr Gly
                485   490   495

Arg Gln Ile Phe Gln Pro Leu His Ala Leu Arg Asn Ala Glu Lys Val
            500   505   510

Leu Leu Pro Gly Tyr His His Phe Glu Trp Gln Pro Pro Leu Lys Asn
        515   520   525

Val Ser Ser Ser Thr Asp Val Gly Ile Ile Asp Gly Leu Ser Gly Leu
    530   535   540

Ser Ser Ser Val Asp Asp Tyr Pro Val Asp Thr Ile Ala Lys Arg Phe
545   550   555   560

Arg Tyr Asp Ser Ala Leu Val Ser Ala Leu Met Asp Met Glu Glu Asp
            565   570   575

Ile Leu Glu Gly Met Arg Ser Gln Asp Leu Asp Asp Tyr Leu Asn Gly
            580   585   590

Pro Phe Thr Val Val Val Lys Glu Ser Cys Asp Gly Met Gly Asp Val
        595   600   605

Ser Glu Lys His Gly Ser Gly Pro Val Val Pro Glu Lys Ala Val Arg
    610   615   620

Phe Ser Phe Thr Ile Met Lys Ile Thr Ile Ala His Ser Ser Gln Asn
625   630   635   640

Val Lys Val Phe Glu Glu Ala Lys Pro Asn Ser Glu Leu Cys Cys Lys
            645   650   655

Pro Leu Cys Leu Met Leu Ala Asp Glu Ser Asp His Glu Thr Leu Thr
        660   665   670

Ala Ile Leu Ser Pro Leu Ile Ala Glu Arg Glu Ala Met Lys Ser Ser
        675   680   685

Glu Leu Met Leu Glu Leu Gly Gly Ile Leu Arg Thr Phe Lys Phe Ile
    690   695   700

Phe Arg Gly Thr Gly Tyr Asp Glu Lys Leu Val Arg Glu Val Glu Gly
705   710   715   720

Leu Glu Ala Ser Gly Ser Val Tyr Ile Cys Thr Leu Cys Asp Ala Thr
              725   730   735

Arg Leu Glu Ala Ser Gln Asn Leu Val Phe His Ser Ile Thr Arg Ser
              740   745   750

His Ala Glu Asn Leu Glu Arg Tyr Glu Val Trp Arg Ser Asn Pro Tyr
        755   760   765

His Glu Ser Val Glu Glu Leu Arg Asp Arg Val Lys Gly Val Ser Ala
    770   775   780

Lys Pro Phe Ile Glu Thr Val Pro Ser Ile Asp Ala Leu His Cys Asp
785   790   795   800

Ile Gly Asn Ala Ala Glu Phe Tyr Lys Ile Phe Gln Leu Glu Ile Gly
              805   810   815

Glu Val Tyr Lys Asn Pro Asn Ala Ser Lys Glu Glu Arg Lys Arg Trp
        820   825   830

Gln Ala Thr Leu Asp Lys His Leu Arg Lys Lys Met Asn Leu Lys Pro
        835   840   845

Ile Met Arg Met Asn Gly Asn Phe Ala Arg Lys Leu Met Thr Lys Glu
    850   855   860

Thr Val Asp Ala Val Cys Glu Leu Ile Pro Ser Glu Glu Arg His Glu
865   870   875   880

Ala Leu Arg Glu Leu Met Asp Leu Tyr Leu Lys Met Lys Pro Val Trp
              885   890   895

Arg Ser Ser Cys Pro Ala Lys Glu Cys Pro Glu Ser Leu Cys Gln Tyr
              900   905   910

Ser Phe Asn Ser Gln Arg Phe Ala Glu Leu Leu Ser Thr Lys Phe Lys
        915   920   925

Tyr Arg Tyr Glu Gly Lys Ile Thr Asn Tyr Phe His Lys Thr Leu Ala
    930   935   940

His Val Pro Glu Ile Ile Glu Arg Asp Gly Ser Ile Gly Ala Trp Ala
945   950   955   960

Ser Glu Gly Asn Glu Ser Gly Asn Lys Leu Phe Arg Arg Phe Arg Lys
                965   970   975

Met Asn Ala Arg Gln Ser Lys Cys Tyr Glu Met Glu Asp Val Leu Lys
                980   985   990

His His Trp Leu Tyr Thr Ser Lys Tyr Leu Gln Lys Phe Met Asn Ala
          995   1000   1005

His Asn Ala Leu Lys Thr Ser Gly Phe Thr Met Asn Pro Gln Ala
    1010   1015   1020

Ser Leu Gly Asp Pro Leu Gly Ile Glu Asp Ser Leu Glu Ser Gln
    1025   1030   1035

Asp Ser Met Glu Phe
    1040

<210> 2453
<211> 527
<212> PRT
<213> Homo sapiens

<400> 2453

Met Ser Leu Gln Met Val Thr Val Ser Asn Asn Ile Ala Leu Ile Gln
1   5   10   15

Pro Gly Phe Ser Leu Met Asn Phe Asp Gly Gln Val Phe Phe Phe Gly
          20   25   30

Gln Lys Gly Trp Pro Lys Arg Ser Cys Pro Thr Gly Val Phe His Leu
          35   40   45

Asp Val Lys His Asn His Val Lys Leu Lys Pro Thr Ile Phe Ser Lys
    50   55   60

Asp Ser Cys Tyr Leu Pro Pro Leu Arg Tyr Pro Ala Thr Cys Thr Phe
65   70   75   80

Lys Gly Ser Leu Glu Ser Glu Lys His Gln Tyr Ile Ile His Gly Gly

```
                          85                      90                      95


Lys Thr Pro Asn Asn Glu Val Ser Asp Lys Ile Tyr Val Met Ser Ile
            100                 105                 110


Val Cys Lys Asn Asn Lys Lys Val Thr Phe Arg Cys Thr Glu Lys Asp
            115                 120                 125


Leu Val Gly Asp Val Pro Glu Ala Arg Tyr Gly His Ser Ile Asn Val
    130                 135                 140


Val Tyr Ser Arg Gly Lys Ser Met Gly Ala Leu Phe Gly Gly Arg Ser
145                 150                 155                 160


Tyr Met Pro Ser Thr His Arg Thr Thr Glu Lys Trp Asn Ser Val Ala
            165                 170                 175


Asp Cys Leu Pro Cys Val Phe Leu Val Asp Phe Glu Phe Gly Cys Ala
            180                 185                 190


Thr Ser Tyr Ile Leu Pro Glu Leu Gln Asp Gly Leu Ser Phe His Val
            195                 200                 205


Ser Ile Ala Lys Asn Asp Thr Ile Tyr Ile Leu Gly Gly His Ser Leu
    210                 215                 220


Ala Asn Asn Ile Arg Pro Ala Asn Leu Tyr Arg Ile Arg Val Asp Leu
225                 230                 235                 240


Pro Leu Gly Ser Pro Ala Val Asn Cys Thr Val Leu Pro Gly Gly Ile
            245                 250                 255


Ser Val Ser Ser Ala Ile Leu Thr Gln Thr Asn Asn Asp Glu Phe Val
            260                 265                 270


Ile Val Gly Gly Tyr Gln Leu Glu Asn Gln Lys Arg Met Ile Cys Asn
            275                 280                 285


Ile Ile Ser Leu Glu Asp Asn Lys Ile Glu Ile Arg Glu Met Glu Thr
    290                 295                 300


Pro Asp Trp Thr Pro Asp Ile Lys His Ser Lys Ile Trp Phe Gly Ser
305                 310                 315                 320


Asn Thr Gly Asn Gly Thr Val Phe Leu Gly Ile Pro Gly Asp Asn Lys
            325                 330                 335
```

```
Gln Val Val Ser Glu Gly Phe Tyr Phe Tyr Met Leu Lys Cys Ala Glu
            340             345             350


Asp Asp Thr Asn Glu Glu Gln Thr Thr Phe Thr Asn Ser Gln Thr Ser
            355             360             365


Thr Glu Asp Pro Gly Asp Ser Thr Pro Phe Glu Asp Ser Glu Glu Phe
    370             375             380


Cys Phe Ser Ala Glu Ala Asn Ser Phe Asp Gly Asp Asp Glu Phe Asp
385             390             395             400


Thr Tyr Asn Glu Asp Asp Glu Glu Asp Glu Ser Glu Thr Gly Tyr Trp
            405             410             415


Ile Thr Cys Cys Pro Thr Cys Asp Val Asp Ile Asn Thr Trp Val Pro
            420             425             430


Phe Tyr Ser Thr Glu Leu Asn Lys Pro Ala Met Ile Tyr Cys Ser His
            435             440             445


Gly Asp Gly His Trp Val His Ala Gln Cys Met Asp Leu Ala Glu Arg
    450             455             460


Thr Leu Ile His Leu Ser Ala Gly Ser Asn Lys Tyr Tyr Cys Asn Glu
465             470             475             480


His Val Glu Ile Ala Arg Ala Leu His Thr Pro Gln Arg Val Leu Pro
            485             490             495


Leu Lys Lys Pro Pro Met Lys Ser Leu Arg Lys Lys Gly Ser Gly Lys
            500             505             510


Ile Leu Thr Pro Ala Lys Lys Ser Phe Leu Arg Arg Leu Phe Asp
            515             520             525


<210> 2454
<211> 93
<212> PRT
<213> Homo sapiens

<400> 2454

Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1               5               10              15
```

```
Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
              20                  25                  30


Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
          35                  40                  45


Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
      50                  55                  60


Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65                  70                  75                  80


Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
                  85                  90
```

```
<210>  2455
<211>  277
<212>  PRT
<213>  Homo sapiens

<400>  2455
```

```
Met Cys Val Gly Ala Arg Arg Leu Gly Arg Gly Pro Cys Ala Ala Leu
1               5                  10                  15


Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
              20                  25                  30


Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
          35                  40                  45


Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
      50                  55                  60


Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65                  70                  75                  80


Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
              85                  90                  95


Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
          100                 105                 110


Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
          115                 120                 125


Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
      130                 135                 140
```

784

```
Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150             155             160


Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165             170             175


Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180             185             190


Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
            195             200             205


Val Pro Gly Gly Arg Ala Val Ala Ala Ile Leu Gly Leu Gly Leu Val
        210             215             220


Leu Gly Leu Leu Gly Pro Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
225             230             235             240


Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
            245             250             255


Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser
            260             265             270


Thr Leu Ala Lys Ile
            275


<210>   2456
<211>   183
<212>   PRT
<213>   Homo sapiens

<400>   2456

Met Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg
1               5               10              15


Pro Arg Phe Glu Arg Asn Lys Leu Leu Leu Val Ala Ser Val Ile Gln
            20              25              30


Gly Leu Gly Leu Leu Leu Cys Phe Thr Tyr Ile Cys Leu His Phe Ser
            35              40              45


Ala Leu Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val
        50              55              60
```

Gln Phe Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln
65   70   75   80

Lys Glu Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn
                85   90   95

Cys Asp Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu
                100   105   110

Val Asn Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln
            115   120   125

Leu Lys Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr
    130   135   140

Tyr Lys Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu
145   150   155   160

Asp Asp Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn
                165   170   175

Pro Gly Glu Phe Cys Val Leu
            180

<210>   2457
<211>   275
<212>   PRT
<213>   Homo sapiens

<400>   2457

Met Leu Ser Leu Leu Leu Leu Ala Leu Pro Val Leu Ala Ser Arg Ala
1   5   10   15

Tyr Ala Ala Pro Ala Pro Val Gln Ala Leu Gln Gln Ala Gly Ile Val
                20   25   30

Gly Gly Gln Glu Ala Pro Arg Ser Lys Trp Pro Trp Gln Val Ser Leu
            35   40   45

Arg Val Arg Asp Arg Tyr Trp Met His Phe Cys Gly Gly Ser Leu Ile
    50   55   60

His Pro Gln Trp Val Leu Thr Ala Ala His Cys Leu Gly Pro Asp Val
65   70   75   80

Lys Asp Leu Ala Thr Leu Arg Val Gln Leu Arg Glu Gln His Leu Tyr
                85   90   95

```
Tyr Gln Asp Gln Leu Leu Pro Val Ser Arg Ile Ile Val His Pro Gln
        100             105             110

Phe Tyr Ile Ile Gln Thr Gly Ala Asp Ile Ala Leu Leu Glu Leu Glu
        115             120             125

Glu Pro Val Asn Ile Ser Ser Arg Val His Thr Val Met Leu Pro Pro
        130             135             140

Ala Ser Glu Thr Phe Pro Pro Gly Met Pro Cys Trp Val Thr Gly Trp
145             150             155             160

Gly Asp Val Asp Asn Asp Glu Pro Leu Pro Pro Phe Pro Leu Lys
                165             170             175

Gln Val Lys Val Pro Ile Met Glu Asn His Ile Cys Asp Ala Lys Tyr
            180             185             190

His Leu Gly Ala Tyr Thr Gly Asp Asp Val Arg Ile Ile Arg Asp Asp
            195             200             205

Met Leu Cys Ala Gly Asn Ser Gln Arg Asp Ser Cys Lys Gly Asp Ser
    210             215             220

Gly Gly Pro Leu Val Cys Lys Val Asn Gly Thr Trp Leu Gln Ala Gly
225             230             235             240

Val Val Ser Trp Asp Glu Gly Cys Ala Gln Pro Asn Arg Pro Gly Ile
            245             250             255

Tyr Thr Arg Val Thr Tyr Tyr Leu Asp Trp Ile His His Tyr Val Pro
            260             265             270

Lys Lys Pro
        275


<210>  2458
<211>  363
<212>  PRT
<213>  Homo sapiens

<400>  2458

Met Ala Gln Thr Pro Ala Phe Asp Lys Pro Lys Val Glu Leu His Val
1               5               10              15
```

His Leu Asp Gly Ser Ile Lys Pro Glu Thr Ile Leu Tyr Tyr Gly Arg
            20   25   30

Arg Arg Gly Ile Ala Leu Pro Ala Asn Thr Ala Glu Gly Leu Leu Asn
            35   40   45

Val Ile Gly Met Asp Lys Pro Leu Thr Leu Pro Asp Phe Leu Ala Lys
    50   55   60

Phe Asp Tyr Tyr Met Pro Ala Ile Ala Gly Cys Arg Glu Ala Ile Lys
65   70   75   80

Arg Ile Ala Tyr Glu Phe Val Glu Met Lys Ala Lys Glu Gly Val Val
                85   90   95

Tyr Val Glu Val Arg Tyr Ser Pro His Leu Leu Ala Asn Ser Lys Val
            100   105   110

Glu Pro Ile Pro Trp Asn Gln Ala Glu Gly Asp Leu Thr Pro Asp Glu
            115   120   125

Val Val Ala Leu Val Gly Gln Gly Leu Gln Glu Gly Glu Arg Asp Phe
    130   135   140

Gly Val Lys Ala Arg Ser Ile Leu Cys Cys Met Arg His Gln Pro Asn
145   150   155   160

Trp Ser Pro Lys Val Val Glu Leu Cys Lys Asn Tyr Gln Gln Gln Thr
            165   170   175

Val Val Ala Ile Asp Leu Ala Gly Asp Glu Thr Ile Pro Gly Ser Ser
            180   185   190

Leu Leu Pro Gly His Val Gln Ala Tyr Gln Glu Ala Val Lys Ser Gly
    195   200   205

Ile His Arg Thr Val His Ala Gly Glu Val Gly Ser Ala Glu Val Val
    210   215   220

Lys Glu Ala Val Asp Ile Leu Lys Thr Glu Arg Leu Gly His Gly Tyr
225   230   235   240

His Thr Leu Glu Asp Gln Ala Leu Tyr Asn Arg Leu Arg Gln Glu Asn
            245   250   255

Met His Phe Glu Ile Cys Pro Trp Ser Ser Tyr Leu Thr Gly Ala Trp

```
                 260                    265                    270


    Lys Pro Asp Thr Glu His Ala Val Ile Arg Leu Lys Asn Asp Gln Ala
            275                    280                    285


    Asn Tyr Ser Leu Asn Thr Asp Asp Pro Leu Ile Phe Lys Ser Thr Leu
        290                    295                    300


    Asp Thr Asp Tyr Gln Met Thr Lys Arg Asp Met Gly Phe Thr Glu Glu
    305                    310                    315                    320


    Glu Phe Lys Arg Leu Asn Ile Asn Ala Ala Lys Ser Ser Phe Leu Pro
                325                    330                    335


    Glu Asp Glu Lys Arg Glu Leu Leu Asp Leu Leu Tyr Lys Ala Tyr Gly
                340                    345                    350


    Met Pro Pro Ser Ala Ser Ala Gly Gln Asn Leu
            355                    360
```

```
<210>  2459
<211>  443
<212>  PRT
<213>  Homo sapiens

<400>  2459
```

```
    Met Asp Phe Pro Cys Leu Trp Leu Gly Leu Leu Leu Pro Leu Val Ala
    1                 5                  10                    15


    Ala Leu Asp Phe Asn Tyr His Arg Gln Glu Gly Met Glu Ala Phe Leu
                20                    25                    30


    Lys Thr Val Ala Gln Asn Tyr Ser Ser Val Thr His Leu His Ser Ile
            35                    40                    45


    Gly Lys Ser Val Lys Gly Arg Asn Leu Trp Val Leu Val Val Gly Arg
        50                    55                    60


    Phe Pro Lys Glu His Arg Ile Gly Ile Pro Glu Phe Lys Tyr Val Ala
    65                    70                    75                    80


    Asn Met His Gly Asp Glu Thr Val Gly Arg Glu Leu Leu Leu His Leu
                85                    90                    95


    Ile Asp Tyr Leu Val Thr Ser Asp Gly Lys Asp Pro Glu Ile Thr Asn
                100                    105                    110
```

```
Leu Ile Asn Ser Thr Arg Ile His Ile Met Pro Ser Met Asn Pro Asp
        115                 120             125

Gly Phe Glu Ala Val Lys Lys Pro Asp Cys Tyr Tyr Ser Ile Gly Arg
    130                 135             140

Glu Asn Tyr Asn Gln Tyr Asp Leu Asn Arg Asn Phe Pro Asp Ala Phe
145                 150             155                 160

Glu Tyr Asn Asn Val Ser Arg Gln Pro Glu Thr Val Ala Val Met Lys
            165             170             175

Trp Leu Lys Thr Glu Thr Phe Val Leu Ser Ala Asn Leu His Gly Gly
        180             185             190

Ala Leu Val Ala Ser Tyr Pro Phe Asp Asn Gly Val Gln Ala Thr Gly
        195             200             205

Ala Leu Tyr Ser Arg Ser Leu Thr Pro Asp Asp Asp Val Phe Gln Tyr
    210             215             220

Leu Ala His Thr Tyr Ala Ser Arg Asn Pro Asn Met Lys Lys Gly Asp
225             230             235                 240

Glu Cys Lys Asn Lys Met Asn Phe Pro Asn Gly Val Thr Asn Gly Tyr
            245             250             255

Ser Trp Tyr Pro Leu Gln Gly Gly Met Gln Asp Tyr Asn Tyr Ile Trp
        260             265             270

Ala Gln Cys Phe Glu Ile Thr Leu Glu Leu Ser Cys Cys Lys Tyr Pro
        275             280             285

Arg Glu Glu Lys Leu Pro Ser Phe Trp Asn Asn Asn Lys Ala Ser Leu
    290             295             300

Ile Glu Tyr Ile Lys Gln Val His Leu Gly Val Lys Gly Gln Val Phe
305             310             315                 320

Asp Gln Asn Gly Asn Pro Leu Pro Asn Val Ile Val Glu Val Gln Asp
            325             330             335

Arg Lys His Ile Cys Pro Tyr Arg Thr Asn Lys Tyr Gly Glu Tyr Tyr
            340             345             350
```

```
Leu Leu Leu Leu Pro Gly Ser Tyr Ile Ile Asn Val Thr Val Pro Gly
        355             360             365
```

```
His Asp Pro His Ile Thr Lys Val Ile Ile Pro Glu Lys Ser Gln Asn
    370             375             380
```

```
Phe Ser Ala Leu Lys Lys Asp Ile Leu Leu Pro Phe Gln Gly Gln Leu
385             390             395             400
```

```
Asp Ser Ile Pro Val Ser Asn Pro Ser Cys Pro Met Ile Pro Leu Tyr
            405             410             415
```

```
Arg Asn Leu Pro Asp His Ser Ala Ala Thr Lys Pro Ser Leu Phe Leu
        420             425             430
```

```
Phe Leu Val Ser Leu Leu His Ile Phe Phe Lys
        435             440
```

```
<210>  2460
<211>  144
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2460
```

```
Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile
1               5               10              15
```

```
Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
            20              25              30
```

```
Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
        35              40              45
```

```
Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
    50              55              60
```

```
Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
65              70              75              80
```

```
Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met
            85              90              95
```

```
Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
            100             105             110
```

```
Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys
        115             120             125
```

```
Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
    130                 135                 140
```

```
<210> 2461
<211> 204
<212> PRT
<213> Homo sapiens
```

```
<400> 2461
```

```
Met Ala Gly Pro Ala Thr Gln Ser Pro Met Lys Leu Met Ala Leu Gln
1               5                   10                  15
```

```
Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
            20                  25                  30
```

```
Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
        35                  40                  45
```

```
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
    50                  55                  60
```

```
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
65                  70                  75                  80
```

```
Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
                85                  90                  95
```

```
Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
            100                 105                 110
```

```
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
        115                 120                 125
```

```
Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
    130                 135                 140
```

```
Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
145                 150                 155                 160
```

```
Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
                165                 170                 175
```

```
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
            180                 185                 190
```

792

```
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
        195             200
```

```
<210>  2462
<211>  224
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2462
```

```
Met Glu Lys Leu Leu Cys Phe Leu Val Leu Thr Ser Leu Ser His Ala
1               5               10              15
```

```
Phe Gly Gln Thr Asp Met Ser Arg Lys Ala Phe Val Phe Pro Lys Glu
            20              25              30
```

```
Ser Asp Thr Ser Tyr Val Ser Leu Lys Ala Pro Leu Thr Lys Pro Leu
        35              40              45
```

```
Lys Ala Phe Thr Val Cys Leu His Phe Tyr Thr Glu Leu Ser Ser Thr
    50              55              60
```

```
Arg Gly Thr Val Phe Ser Arg Met Pro Pro Arg Asp Lys Thr Met Arg
65              70              75              80
```

```
Phe Phe Ile Phe Trp Ser Lys Asp Ile Gly Tyr Ser Phe Thr Val Gly
                85              90              95
```

```
Gly Ser Glu Ile Leu Phe Glu Val Pro Glu Val Thr Val Ala Pro Val
            100             105             110
```

```
His Ile Cys Thr Ser Trp Glu Ser Ala Ser Gly Ile Val Glu Phe Trp
            115             120             125
```

```
Val Asp Gly Lys Pro Arg Val Arg Lys Ser Leu Lys Lys Gly Tyr Thr
    130             135             140
```

```
Val Gly Ala Glu Ala Ser Ile Ile Leu Gly Gln Glu Gln Asp Ser Phe
145             150             155             160
```

```
Gly Gly Asn Phe Glu Gly Ser Gln Ser Leu Val Gly Asp Ile Gly Asn
                165             170             175
```

```
Val Asn Met Trp Asp Phe Val Leu Ser Pro Asp Glu Ile Asn Thr Ile
            180             185             190
```

```
Tyr Leu Gly Gly Pro Phe Ser Pro Asn Val Leu Asn Trp Arg Ala Leu
        195             200             205
```

```
Lys Tyr Glu Val Gln Gly Glu Val Phe Thr Lys Pro Gln Leu Trp Pro
    210                 215             220
```

<210>   2463
<211>   993
<212>   PRT
<213>   Homo sapiens

<400>   2463

```
Met Pro Ala Leu Ala Arg Asp Ala Gly Thr Val Pro Leu Leu Val Val
1               5               10              15


Phe Ser Ala Met Ile Phe Gly Thr Ile Thr Asn Gln Asp Leu Pro Val
            20              25              30


Ile Lys Cys Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly
        35              40              45


Lys Ser Ser Ser Tyr Pro Met Val Ser Glu Ser Pro Glu Asp Leu Gly
    50              55              60


Cys Ala Leu Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Ala
65              70              75              80


Val Glu Val Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp
            85              90              95


Ala Pro Gly Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu
            100             105             110


Asn Cys Gln Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met
        115             120             125


Val Ile Leu Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe
    130             135             140


Ile Gln Ser Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile
145             150             155             160


Arg Asn Thr Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met
            165             170             175


Glu Asn Gln Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro
            180             185             190
```

Ile Val Glu Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu
          195   200   205

Glu Ser Pro Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu
    210   215   220

Phe Gly Thr Asp Ile Arg Cys Cys Ala Arg Asn Glu Leu Gly Arg Glu
225   230   235   240

Cys Thr Arg Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr
              245   250   255

Leu Pro Gln Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys
              260   265   270

Lys Ala Val His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu
          275   280   285

Asn Lys Ala Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser
290   295   300

Thr Asn Arg Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val
305   310   315   320

Ala Arg Asn Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro
              325   330   335

Ser Gln Ser Ala Leu Val Thr Ile Val Gly Lys Gly Phe Ile Asn Ala
          340   345   350

Thr Asn Ser Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys
          355   360   365

Phe Ser Val Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr
370   375   380

Phe Ser Arg Lys Ser Phe Pro Cys Glu Gln Lys Gly Leu Asp Asn Gly
385   390   395   400

Tyr Ser Ile Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr
              405   410   415

Ile Phe His Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr
              420   425   430

Leu Asn Ile Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser

```
                435                     440                     445


    Gln Ala Ser Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp
        450             455             460


    Lys Lys Cys Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu
    465             470             475                     480


    Gly Val Trp Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val
                485             490             495


    Ser Ser Ser Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val
                500             505             510


    Lys Cys Cys Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu
            515             520             525


    Leu Asn Ser Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Ile Ser Phe
        530             535             540


    Tyr Ala Thr Ile Gly Val Cys Leu Leu Phe Ile Val Val Leu Thr Leu
    545             550             555                     560


    Leu Ile Cys His Lys Tyr Lys Lys Gln Phe Arg Tyr Glu Ser Gln Leu
                565             570             575


    Gln Met Val Gln Val Thr Gly Ser Ser Asp Asn Glu Tyr Phe Tyr Val
                580             585             590


    Asp Phe Arg Glu Tyr Glu Tyr Asp Leu Lys Trp Glu Phe Pro Arg Glu
                595             600             605


    Asn Leu Glu Phe Gly Lys Val Leu Gly Ser Gly Ala Phe Gly Lys Val
        610             615             620


    Met Asn Ala Thr Ala Tyr Gly Ile Ser Lys Thr Gly Val Ser Ile Gln
    625             630             635                     640


    Val Ala Val Lys Met Leu Lys Glu Lys Ala Asp Ser Ser Glu Arg Glu
                645             650             655


    Ala Leu Met Ser Glu Leu Lys Met Met Thr Gln Leu Gly Ser His Glu
                660             665             670


    Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Leu Ser Gly Pro Ile Tyr
        675             680             685
```

```
Leu Ile Phe Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Tyr Leu Arg
    690             695             700

Ser Lys Arg Glu Lys Phe His Arg Thr Trp Thr Glu Ile Phe Lys Glu
705             710             715             720

His Asn Phe Ser Phe Tyr Pro Thr Phe Gln Ser His Pro Asn Ser Ser
            725             730             735

Met Pro Gly Ser Arg Glu Val Gln Ile His Pro Asp Ser Asp Gln Ile
            740             745             750

Ser Gly Leu His Gly Asn Ser Phe His Ser Glu Asp Glu Ile Glu Tyr
            755             760             765

Glu Asn Gln Lys Arg Leu Glu Glu Glu Asp Leu Asn Val Leu Thr
    770             775             780

Phe Glu Asp Leu Leu Cys Phe Ala Tyr Gln Val Ala Lys Gly Met Glu
785             790             795             800

Phe Leu Glu Phe Lys Ser Cys Val His Arg Asp Leu Ala Ala Arg Asn
            805             810             815

Val Leu Val Thr His Gly Lys Val Val Lys Ile Cys Asp Phe Gly Leu
            820             825             830

Ala Arg Asp Ile Met Ser Asp Ser Asn Tyr Val Val Arg Gly Asn Ala
    835             840             845

Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Leu Phe Glu Gly Ile
    850             855             860

Tyr Thr Ile Lys Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu
865             870             875             880

Ile Phe Ser Leu Gly Val Asn Pro Tyr Pro Gly Ile Pro Val Asp Ala
            885             890             895

Asn Phe Tyr Lys Leu Ile Gln Asn Gly Phe Lys Met Asp Gln Pro Phe
            900             905             910

Tyr Ala Thr Glu Glu Ile Tyr Ile Ile Met Gln Ser Cys Trp Ala Phe
            915             920             925
```

797

Asp Ser Arg Lys Arg Pro Ser Phe Pro Asn Leu Thr Ser Phe Leu Gly
    930   935   940

Cys Gln Leu Ala Asp Ala Glu Glu Ala Met Tyr Gln Asn Val Asp Gly
945   950   955   960

Arg Val Ser Glu Cys Pro His Thr Tyr Gln Asn Arg Arg Pro Phe Ser
                965   970   975

Arg Glu Met Asp Leu Gly Leu Leu Ser Pro Gln Ala Gln Val Glu Asp
            980   985   990

Ser

<210> 2464
<211> 443
<212> PRT
<213> Homo sapiens

<400> 2464

Met Glu Val Thr Ala Asp Gln Pro Arg Trp Val Ser His His His Pro
1   5   10   15

Ala Val Leu Asn Gly Gln His Pro Asp Thr His His Pro Gly Leu Ser
            20   25   30

His Ser Tyr Met Asp Ala Ala Gln Tyr Pro Leu Pro Glu Glu Val Asp
        35   40   45

Val Leu Phe Asn Ile Asp Gly Gln Gly Asn His Val Pro Pro Tyr Tyr
    50   55   60

Gly Asn Ser Val Arg Ala Thr Val Gln Arg Tyr Pro Pro Thr His His
65   70   75   80

Gly Ser Gln Val Cys Arg Pro Pro Leu Leu His Gly Ser Leu Pro Trp
            85   90   95

Leu Asp Gly Gly Lys Ala Leu Gly Ser His His Thr Ala Ser Pro Trp
            100   105   110

Asn Leu Ser Pro Phe Ser Lys Thr Ser Ile His His Gly Ser Pro Gly
        115   120   125

Pro Leu Ser Val Tyr Pro Pro Ala Ser Ser Ser Ser Leu Ser Gly Gly

         130   135   140

    His Ala Ser Pro His Leu Phe Thr Phe Pro Pro Thr Pro Pro Lys Asp
    145   150   155   160

    Val Ser Pro Asp Pro Ser Leu Ser Thr Pro Gly Ser Ala Gly Ser Ala
                    165   170   175

    Arg Gln Asp Glu Lys Glu Cys Leu Lys Tyr Gln Val Pro Leu Pro Asp
                180   185   190

    Ser Met Lys Leu Glu Ser Ser His Ser Arg Gly Ser Met Thr Ala Leu
            195   200   205

    Gly Gly Ala Ser Ser Ser Thr His His Pro Ile Thr Thr Tyr Pro Pro
    210   215   220

                    /
    Tyr Val Pro Glu Tyr Ser Ser Gly Leu Phe Pro Pro Ser Ser Leu Leu
    225   230   235   240

    Gly Gly Ser Pro Thr Gly Phe Gly Cys Lys Ser Arg Pro Lys Ala Arg
                    245   250   255

    Ser Ser Thr Gly Arg Glu Cys Val Asn Cys Gly Ala Thr Ser Thr Pro
                260   265   270

    Leu Trp Arg Arg Asp Gly Thr Gly His Tyr Leu Cys Asn Ala Cys Gly
            275   280   285

    Leu Tyr His Lys Met Asn Gly Gln Asn Arg Pro Leu Ile Lys Pro Lys
        290   295   300

    Arg Arg Leu Ser Ala Ala Arg Arg Ala Gly Thr Ser Cys Ala Asn Cys
    305   310   315   320

    Gln Thr Thr Thr Thr Thr Leu Trp Arg Arg Asn Ala Asn Gly Asp Pro
                    325   330   335

    Val Cys Asn Ala Cys Gly Leu Tyr Tyr Lys Leu His Asn Ile Asn Arg
                340   345   350

    Pro Leu Thr Met Lys Lys Glu Gly Ile Gln Thr Arg Asn Arg Lys Met
            355   360   365

    Ser Ser Lys Ser Lys Lys Cys Lys Lys Val His Asp Ser Leu Glu Asp
        370   375   380

                                    799

```
Phe Pro Lys Asn Ser Ser Phe Asn Pro Ala Ala Leu Ser Arg His Met
385                 390             395                 400


Ser Ser Leu Ser His Ile Ser Pro Phe Ser His Ser Ser His Met Leu
                405             410                 415


Thr Thr Pro Thr Pro Met His Pro Pro Ser Ser Leu Ser Phe Gly Pro
            420             425                 430


His His Pro Ser Ser Met Val Thr Ala Met Gly
        435             440
```

```
<210>  2465
<211>  459
<212>  PRT
<213>  Homo sapiens

<400>  2465
```

```
Met Thr Ile Leu Gly Thr Thr Phe Gly Met Val Phe Ser Leu Leu Gln
1               5               10              15


Val Val Ser Gly Glu Ser Gly Tyr Ala Gln Asn Gly Asp Leu Glu Asp
            20              25              30


Ala Glu Leu Asp Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val
        35              40              45


Asn Gly Ser Gln His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val
    50              55              60


Asn Ile Thr Asn Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val
65              70              75              80


Lys Cys Leu Asn Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr
            85              90              95


Lys Lys Phe Leu Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly
            100             105             110


Glu Lys Ser Leu Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys
        115             120             125


Pro Glu Ala Pro Phe Asp Leu Ser Val Val Tyr Arg Glu Gly Ala Asn
    130             135             140
```

Asp Phe Val Val Thr Phe Asn Thr Ser His Leu Gln Lys Lys Tyr Val
145   150   155   160

Lys Val Leu Met His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn
                165   170   175

Lys Trp Thr His Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln
            180   185   190

Arg Lys Leu Gln Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile
        195   200   205

Pro Asp His Tyr Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr
    210   215   220

Tyr Phe Arg Thr Pro Glu Ile Asn Asn Ser Ser Gly Glu Met Asp Pro
225   230   235   240

Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu Leu
                245   250   255

Val Ile Leu Ala Cys Val Leu Trp Lys Lys Arg Ile Lys Pro Ile Val
            260   265   270

Trp Pro Ser Leu Pro Asp His Lys Lys Thr Leu Glu His Leu Cys Lys
        275   280   285

Lys Pro Arg Lys Asn Leu Asn Val Ser Phe Asn Pro Glu Ser Phe Leu
    290   295   300

Asp Cys Gln Ile His Arg Val Asp Asp Ile Gln Ala Arg Asp Glu Val
305   310   315   320

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
                325   330   335

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
                340   345   350

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
        355   360   365

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
    370   375   380

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val

```
       385                    390                    395                    400
```

```
       Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
                       405                 410                 415
```

```
       Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
                       420                 425                 430
```

```
       Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
                   435                 440                 445
```

```
       Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
           450                 455
```

```
<210>  2466
<211>  362
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2466
```

```
       Met Ala Thr Ala Glu Thr Ala Leu Pro Ser Ile Ser Thr Leu Thr Ala
       1               5                   10                  15
```

```
       Leu Gly Pro Phe Pro Asp Thr Gln Asp Asp Phe Leu Lys Trp Trp Arg
                       20                  25                  30
```

```
       Ser Glu Glu Ala Gln Asp Met Gly Pro Gly Pro Pro Asp Pro Thr Glu
                   35                  40                  45
```

```
       Pro Pro Leu His Val Lys Ser Glu Asp Gln Pro Gly Glu Glu Glu Asp
           50                  55                  60
```

```
       Asp Glu Arg Gly Ala Asp Ala Thr Trp Asp Leu Asp Leu Leu Leu Thr
       65                  70                  75                  80
```

```
       Asn Phe Ser Gly Pro Glu Pro Gly Gly Ala Pro Gln Thr Cys Ala Leu
                       85                  90                  95
```

```
       Ala Pro Ser Glu Ala Ser Gly Ala Gln Tyr Pro Pro Pro Glu Thr
                   100                 105                 110
```

```
       Leu Gly Ala Tyr Ala Gly Gly Pro Gly Leu Val Ala Gly Leu Leu Gly
                   115                 120                 125
```

```
       Ser Glu Asp His Ser Gly Trp Val Arg Pro Ala Leu Arg Ala Arg Ala
           130                 135                 140
```

```
Pro Asp Ala Phe Val Gly Pro Ala Leu Ala Pro Ala Pro Ala Pro Glu
145             150             155             160


Pro Lys Ala Leu Ala Leu Gln Pro Val Tyr Pro Gly Pro Gly Ala Gly
                165             170             175


Ser Ser Gly Gly Tyr Phe Pro Arg Thr Gly Leu Ser Val Pro Ala Ala
            180             185             190


Ser Gly Ala Pro Tyr Gly Leu Leu Ser Gly Tyr Pro Ala Met Tyr Pro
            195             200             205


Ala Pro Gln Tyr Gln Gly His Phe Gln Leu Phe Arg Gly Leu Gln Gly
    210             215             220


Pro Ala Pro Gly Pro Ala Thr Ser Pro Ser Phe Leu Ser Cys Leu Gly
225             230             235             240


Pro Gly Thr Val Gly Thr Gly Leu Gly Gly Thr Ala Glu Asp Pro Gly
            245             250             255


Val Ile Ala Glu Thr Ala Pro Ser Lys Arg Gly Arg Arg Ser Trp Ala
            260             265             270


Arg Lys Arg Gln Ala Ala His Thr Cys Ala His Pro Gly Cys Gly Lys
    275             280             285


Ser Tyr Thr Lys Ser Ser His Leu Lys Ala His Leu Arg Thr His Thr
290             295             300


Gly Glu Lys Pro Tyr Ala Cys Thr Trp Glu Gly Cys Gly Trp Arg Phe
305             310             315             320


Ala Arg Ser Asp Glu Leu Thr Arg His Tyr Arg Lys His Thr Gly Gln
            325             330             335


Arg Pro Phe Arg Cys Gln Leu Cys Pro Arg Ala Phe Ser Arg Ser Asp
            340             345             350


His Leu Ala Leu His Met Lys Arg His Leu
            355             360
```

```
<210>  2467
<211>  509
<212>  PRT
<213>  Homo sapiens
```

<400> 2467

```
Met Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn
1               5                   10                  15


Ile Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly
            20                  25                  30


Lys Gly Thr Leu Leu Ile Arg Asn Gly Ser Glu Val Arg Asp Pro Leu
        35                  40                  45


Val Thr Tyr Glu Gly Ser Asn Pro Pro Ala Ser Pro Leu Gln Asp Asn
    50                  55                  60


Leu Val Ile Ala Leu His Ser Tyr Glu Pro Ser His Asp Gly Asp Leu
65                  70                  75                  80


Gly Phe Glu Lys Gly Glu Pro Leu Arg Ile Leu Glu Gln Ser Gly Glu
                85                  90                  95


Trp Trp Lys Ala Gln Ser Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro
            100                 105                 110


Phe Asn Phe Val Ala Lys Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe
        115                 120                 125


Phe Lys Asn Leu Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro
    130                 135                 140


Gly Asn Thr His Gly Ser Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala
145                 150                 155                 160


Gly Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Gln Asn Gln Gly Glu
                165                 170                 175


Val Val Lys His Tyr Lys Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr
            180                 185                 190


Ile Ser Pro Arg Ile Thr Phe Pro Gly Leu His Glu Leu Val Arg His
        195                 200                 205


Tyr Thr Asn Ala Ser Asp Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys
    210                 215                 220


Gln Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val
225                 230                 235                 240
```

```
Pro Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe
              245                 250                 255

Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val
              260                 265                 270

Lys Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu
         275                 280                 285

Ala Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr
    290                 295                 300

Ala Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu
305                 310                 315                 320

Asn Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu
              325                 330                 335

Thr Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met
              340                 345                 350

Ala Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala
         355                 360                 365

Asn Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly
    370                 375                 380

Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala
385                 390                 395                 400

Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr
              405                 410                 415

Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu
              420                 425                 430

Ile Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu
              435                 440                 445

Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn
    450                 455                 460

Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg
465                 470                 475                 480
```

```
Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp
                485                 490                 495

Phe Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro
            500                 505
```

```
<210>  2468
<211>  399
<212>  PRT
<213>  Homo sapiens

<400>  2468
```

```
Met Pro Gln Leu Ser Gly Gly Gly Gly Gly Gly Gly Asp Pro Glu
1               5                 10                  15

Leu Cys Ala Thr Asp Glu Met Ile Pro Phe Lys Asp Glu Gly Asp Pro
            20                  25                  30

Gln Lys Glu Lys Ile Phe Ala Glu Ile Ser His Pro Glu Glu Glu Gly
        35                  40                  45

Asp Leu Ala Asp Ile Lys Ser Ser Leu Val Asn Glu Ser Glu Ile Ile
    50                  55                  60

Pro Ala Ser Asn Gly His Glu Val Ala Arg Gln Ala Gln Thr Ser Gln
65                  70                  75                  80

Glu Pro Tyr His Asp Lys Ala Arg Glu His Pro Asp Asp Gly Lys His
                85                  90                  95

Pro Asp Gly Gly Leu Tyr Asn Lys Gly Pro Ser Tyr Ser Ser Tyr Ser
            100                 105                 110

Gly Tyr Ile Met Met Pro Asn Met Asn Asn Asp Pro Tyr Met Ser Asn
        115                 120                 125

Gly Ser Leu Ser Pro Pro Ile Pro Arg Thr Ser Asn Lys Val Pro Val
    130                 135                 140

Val Gln Pro Ser His Ala Val His Pro Leu Thr Pro Leu Ile Thr Tyr
145                 150                 155                 160

Ser Asp Glu His Phe Ser Pro Gly Ser His Pro Ser His Ile Pro Ser
                165                 170                 175

Asp Val Asn Ser Lys Gln Gly Met Ser Arg His Pro Pro Ala Pro Asp
```

```
                180                   185                   190
```

Ile Pro Thr Phe Tyr Pro Leu Ser Pro Gly Gly Val Gly Gln Ile Thr
        195   200   205

Pro Pro Leu Gly Trp Gln Gly Gln Pro Val Tyr Pro Ile Thr Gly Gly
        210   215   220

Phe Arg Gln Pro Tyr Pro Ser Ser Leu Ser Val Asp Thr Ser Met Ser
225   230   235   240

Arg Phe Ser His His Met Ile Pro Gly Pro Pro Gly Pro His Thr Thr
                245   250   255

Gly Ile Pro His Pro Ala Ile Val Thr Pro Gln Val Lys Gln Glu His
            260   265   270

Pro His Thr Asp Ser Asp Leu Met His Val Lys Pro Gln His Glu Gln
        275   280   285

Arg Lys Glu Gln Glu Pro Lys Arg Pro His Ile Lys Lys Pro Leu Asn
    290   295   300

Ala Phe Met Leu Tyr Met Lys Glu Met Arg Ala Asn Val Val Ala Glu
305   310   315   320

Cys Thr Leu Lys Glu Ser Ala Ala Ile Asn Gln Ile Leu Gly Arg Arg
                325   330   335

Trp His Ala Leu Ser Arg Glu Glu Gln Ala Lys Tyr Tyr Glu Leu Ala
            340   345   350

Arg Lys Glu Arg Gln Leu His Met Gln Leu Tyr Pro Gly Trp Ser Ala
        355   360   365

Arg Asp Asn Tyr Gly Lys Lys Lys Arg Lys Arg Glu Lys Leu Gln
    370   375   380

Glu Ser Ala Ser Gly Thr Gly Pro Arg Met Thr Ala Ala Tyr Ile
385   390   395

<210>   2469
<211>   335
<212>   PRT
<213>   Homo sapiens

<400>   2469

```
Met Gly His Pro Pro Leu Leu Pro Leu Leu Leu Leu Leu His Thr Cys
1               5               10              15

Val Pro Ala Ser Trp Gly Leu Arg Cys Met Gln Cys Lys Thr Asn Gly
            20              25              30

Asp Cys Arg Val Glu Glu Cys Ala Leu Gly Gln Asp Leu Cys Arg Thr
        35              40              45

Thr Ile Val Arg Leu Trp Glu Glu Gly Glu Glu Leu Glu Leu Val Glu
    50              55              60

Lys Ser Cys Thr His Ser Glu Lys Thr Asn Arg Thr Leu Ser Tyr Arg
65              70              75              80

Thr Gly Leu Lys Ile Thr Ser Leu Thr Glu Val Val Cys Gly Leu Asp
            85              90              95

Leu Cys Asn Gln Gly Asn Ser Gly Arg Ala Val Thr Tyr Ser Arg Ser
        100             105             110

Arg Tyr Leu Glu Cys Ile Ser Cys Gly Ser Ser Asp Met Ser Cys Glu
    115             120             125

Arg Gly Arg His Gln Ser Leu Gln Cys Arg Ser Pro Glu Glu Gln Cys
    130             135             140

Leu Asp Val Val Thr His Trp Ile Gln Glu Gly Glu Glu Gly Arg Pro
145             150             155             160

Lys Asp Asp Arg His Leu Arg Gly Cys Gly Tyr Leu Pro Gly Cys Pro
            165             170             175

Gly Ser Asn Gly Phe His Asn Asn Asp Thr Phe His Phe Leu Lys Cys
            180             185             190

Cys Asn Thr Thr Lys Cys Asn Glu Gly Pro Ile Leu Glu Leu Glu Asn
    195             200             205

Leu Pro Gln Asn Gly Arg Gln Cys Tyr Ser Cys Lys Gly Asn Ser Thr
    210             215             220

His Gly Cys Ser Ser Glu Glu Thr Phe Leu Ile Asp Cys Arg Gly Pro
225             230             235             240
```

```
Met Asn Gln Cys Leu Val Ala Thr Gly Thr His Glu Pro Lys Asn Gln
            245                 250                 255

Ser Tyr Met Val Arg Gly Cys Ala Thr Ala Ser Met Cys Gln His Ala
            260                 265                 270

His Leu Gly Asp Ala Phe Ser Met Asn His Ile Asp Val Ser Cys Cys
            275                 280                 285

Thr Lys Ser Gly Cys Asn His Pro Asp Leu Asp Val Gln Tyr Arg Ser
            290                 295                 300

Gly Ala Ala Pro Gln Pro Gly Pro Ala His Leu Ser Leu Thr Ile Thr
305                 310                 315                 320

Leu Leu Met Thr Ala Arg Leu Trp Gly Gly Thr Leu Leu Trp Thr
            325                 330                 335
```

<210> 2470
<211> 285
<212> PRT
<213> Homo sapiens

<400> 2470

```
Met Asp Asp Ser Thr Glu Arg Glu Gln Ser Arg Leu Thr Ser Cys Leu
1               5                   10                  15

Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
            20                  25                  30

Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
            35                  40                  45

Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
            50                  55                  60

Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
65                  70                  75                  80

Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
                85                  90                  95

Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
            100                 105                 110

Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
            115                 120                 125
```

```
Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Val Thr Gln
    130             135         140
```

```
Asp Cys Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys
145             150         155                     160
```

```
Gly Ser Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser
            165         170                 175
```

```
Ala Leu Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr
        180             185                 190
```

```
Phe Phe Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met
        195             200                 205
```

```
Gly His Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu
    210             215                 220
```

```
Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu
225             230             235                     240
```

```
Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly
            245             250                     255
```

```
Asp Glu Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu
        260             265                 270
```

```
Asp Gly Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
        275             280                 285
```

```
<210>  2471
<211>  99
<212>  PRT
<213>  Homo sapiens

<400>  2471
```

```
Met Thr Ser Lys Leu Ala Val Ala Leu Leu Ala Ala Phe Leu Ile Ser
1             5               10                  15
```

```
Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu
            20          25                  30
```

```
Arg Cys Gln Cys Ile Lys Thr Tyr Ser Lys Pro Phe His Pro Lys Phe
        35              40                  45
```

```
Ile Lys Glu Leu Arg Val Ile Glu Ser Gly Pro His Cys Ala Asn Thr
    50                  55                  60
```

```
Glu Ile Ile Val Lys Leu Ser Asp Gly Arg Glu Leu Cys Leu Asp Pro
65                  70                  75                  80
```

```
Lys Glu Asn Trp Val Gln Arg Val Val Glu Lys Phe Leu Lys Arg Ala
                85                  90                  95
```

```
Glu Asn Ser
```

```
<210>  2472
<211>  247
<212>  PRT
<213>  Homo sapiens

<400>  2472
```

```
Met Gln Pro Ile Leu Leu Leu Leu Ala Phe Leu Leu Leu Pro Arg Ala
1               5                   10                  15
```

```
Asp Ala Gly Glu Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg
                20                  25                  30
```

```
Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg
        35                  40                  45
```

```
Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His
    50                  55                  60
```

```
Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys
65                  70                  75                  80
```

```
Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro
                85                  90                  95
```

```
His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu
                100                 105                 110
```

```
Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg
        115                 120                 125
```

```
Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val
    130                 135                 140
```

```
Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu
145                 150                 155                 160
```

```
Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp
                165             170             175

Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val Gly Asp Pro
            180             185             190

Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val
        195             200             205

Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly
    210             215             220

Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val His Trp Ile
225             230             235             240

Lys Lys Thr Met Lys Arg Tyr
                245
```

```
<210> 2473
<211> 281
<212> PRT
<213> Homo sapiens

<400> 2473
```

```
Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1               5               10              15

Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
            20              25              30

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
        35              40              45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Leu Pro
    50              55              60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65              70              75              80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
            85              90              95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
            100             105             110
```

```
Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
        115                 120                 125

Lys Gln Ile Gly His Pro Ser Pro Pro Glu Lys Lys Glu Leu Arg
        130                 135                 140

Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
145                 150                 155                 160

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
                165                 170                 175

Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
                180                 185                 190

Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
        195                 200                 205

His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
    210                 215                 220

Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
225                 230                 235                 240

Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
                245                 250                 255

Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
                260                 265                 270

Gln Thr Phe Phe Gly Leu Tyr Lys Leu
        275                 280
```

```
<210>  2474
<211>  830
<212>  PRT
<213>  Homo sapiens

<400>  2474
```

```
Met Gly Ser Met Phe Arg Ser Glu Glu Val Ala Leu Val Gln Leu Phe
1               5                   10                  15

Leu Pro Thr Ala Ala Ala Tyr Thr Cys Val Ser Arg Leu Gly Glu Leu
            20                  25                  30

Gly Leu Val Glu Phe Arg Asp Leu Asn Ala Ser Val Ser Ala Phe Gln
        35                  40                  45
```

Arg Arg Phe Val Val Asp Val Arg Arg Cys Glu Glu Leu Glu Lys Thr
    50   55   60

Phe Thr Phe Leu Gln Glu Glu Val Arg Arg Ala Gly Leu Val Leu Pro
65   70   75   80

Pro Pro Lys Gly Arg Leu Pro Ala Pro Pro Arg Asp Leu Leu Arg
            85   90   95

Ile Gln Glu Glu Thr Glu Arg Leu Ala Gln Glu Leu Arg Asp Val Arg
        100   105   110

Gly Asn Gln Gln Ala Leu Arg Ala Gln Leu His Gln Leu Gln Leu His
    115   120   125

Ala Ala Val Leu Arg Gln Gly His Glu Pro Gln Leu Ala Ala Ala His
    130   135   140

Thr Asp Gly Ala Ser Glu Arg Thr Pro Leu Leu Gln Ala Pro Gly Gly
145   150   155   160

Pro His Gln Asp Leu Arg Val Asn Phe Val Ala Gly Ala Val Glu Pro
            165   170   175

His Lys Ala Pro Ala Leu Glu Arg Leu Leu Trp Arg Ala Cys Arg Gly
            180   185   190

Phe Leu Ile Ala Ser Phe Arg Glu Leu Glu Gln Pro Leu Glu His Pro
    195   200   205

Val Thr Gly Glu Pro Ala Thr Trp Met Thr Phe Leu Ile Ser Tyr Trp
    210   215   220

Gly Glu Gln Ile Gly Gln Lys Ile Arg Lys Ile Thr Asp Cys Phe His
225   230   235   240

Cys His Val Phe Pro Phe Leu Gln Gln Glu Glu Ala Arg Leu Gly Ala
            245   250   255

Leu Gln Gln Leu Gln Gln Gln Ser Gln Glu Leu Gln Glu Val Leu Gly
    260   265   270

Glu Thr Glu Arg Phe Leu Ser Gln Val Leu Gly Arg Val Leu Gln Leu
    275   280   285

814

Leu Pro Pro Gly Gln Val Gln Val His Lys Met Lys Ala Val Tyr Leu
    290   295   300

Ala Leu Asn Gln Cys Ser Val Ser Thr Thr His Lys Cys Leu Ile Ala
305   310   315   320

Glu Ala Trp Cys Ser Val Arg Asp Leu Pro Ala Leu Gln Glu Ala Leu
            325   330   335

Arg Asp Ser Ser Met Glu Glu Gly Val Ser Ala Val Ala His Arg Ile
            340   345   350

Pro Cys Arg Asp Met Pro Pro Thr Leu Ile Arg Thr Asn Arg Phe Thr
    355   360   365

Ala Ser Phe Gln Gly Ile Val Asp Ala Tyr Gly Val Gly Arg Tyr Gln
    370   375   380

Glu Val Asn Pro Ala Pro Tyr Thr Ile Ile Thr Phe Pro Phe Leu Phe
385   390   395   400

Ala Val Met Phe Gly Asp Val Gly His Gly Leu Leu Met Phe Leu Phe
            405   410   415

Ala Leu Ala Met Val Leu Ala Glu Asn Arg Pro Ala Val Lys Ala Ala
            420   425   430

Gln Asn Glu Ile Trp Gln Thr Phe Phe Arg Gly Arg Tyr Leu Leu Leu
            435   440   445

Leu Met Gly Leu Phe Ser Ile Tyr Thr Gly Phe Ile Tyr Asn Glu Cys
    450   455   460

Phe Ser Arg Ala Thr Ser Ile Phe Pro Ser Gly Trp Ser Val Ala Ala
465   470   475   480

Met Ala Asn Gln Ser Gly Trp Ser Asp Ala Phe Leu Ala Gln His Thr
            485   490   495

Met Leu Thr Leu Asp Pro Asn Val Thr Gly Val Phe Leu Gly Pro Tyr
            500   505   510

Pro Phe Gly Ile Asp Pro Ile Trp Ser Leu Ala Ala Asn His Leu Ser
    515   520   525

Phe Leu Asn Ser Phe Lys Met Lys Met Ser Val Ile Leu Gly Val Val
    530   535   540

His Met Ala Phe Gly Val Val Leu Gly Val Phe Asn His Val His Phe
545   550   555   560

Gly Gln Arg His Arg Leu Leu Leu Glu Thr Leu Pro Glu Leu Thr Phe
            565   570   575

Leu Leu Gly Leu Phe Gly Tyr Leu Val Phe Leu Val Ile Tyr Lys Trp
            580   585   590

Leu Cys Val Trp Ala Ala Arg Ala Ala Ser Ala Pro Ser Ile Leu Ile
        595   600   605

His Phe Ile Asn Met Phe Leu Phe Ser His Ser Pro Ser Asn Arg Leu
    610   615   620

Leu Tyr Pro Arg Gln Glu Val Val Gln Ala Thr Leu Val Val Leu Ala
625   630   635   640

Leu Ala Met Val Pro Ile Leu Leu Leu Gly Thr Pro Leu His Leu Leu
            645   650   655

His Arg His Arg Arg Arg Leu Arg Arg Arg Pro Ala Asp Arg Gln Glu
            660   665   670

Glu Asn Lys Ala Gly Leu Leu Asp Leu Pro Asp Ala Ser Val Asn Gly
    675   680   685

Trp Ser Ser Asp Glu Glu Lys Ala Gly Gly Leu Asp Asp Glu Glu Glu
    690   695   700

Ala Glu Leu Val Pro Ser Glu Val Leu Met His Gln Ala Ile His Thr
705   710   715   720

Ile Glu Phe Cys Leu Gly Cys Val Ser Asn Thr Ala Ser Tyr Leu Arg
            725   730   735

Leu Trp Ala Leu Ser Leu Ala His Ala Gln Leu Ser Glu Val Leu Trp
            740   745   750

Ala Met Val Met Arg Ile Gly Leu Gly Leu Gly Arg Glu Val Gly Val
    755   760   765

Ala Ala Val Val Leu Val Pro Ile Phe Ala Ala Phe Ala Val Met Thr

816

```
              770                    775                      780


    Val Ala Ile Leu Leu Val Met Glu Gly Leu Ser Ala Phe Leu His Ala
    785                 790                 795                 800


    Leu Arg Leu His Trp Val Glu Phe Gln Asn Lys Phe Tyr Ser Gly Thr
                    805                 810                 815


    Gly Tyr Lys Leu Ser Pro Phe Thr Phe Ala Ala Thr Asp Asp
                820                 825                 830
```

```
<210>  2475
<211>  555
<212>  PRT
<213>  Homo sapiens

<400>  2475

    Met Ala Ala Arg Leu Leu Leu Leu Gly Ile Leu Leu Leu Leu Pro
    1               5                   10                  15


    Leu Pro Val Pro Ala Pro Cys His Thr Ala Ala Arg Ser Glu Cys Lys
                    20              25                  30


    Arg Ser His Lys Phe Val Pro Gly Ala Trp Leu Ala Gly Glu Gly Val
                35                  40                  45


    Asp Val Thr Ser Leu Arg Arg Ser Gly Ser Phe Pro Val Asp Thr Gln
        50                  55                  60


    Arg Phe Leu Arg Pro Asp Gly Thr Cys Thr Leu Cys Glu Asn Ala Leu
    65                  70                  75                  80


    Gln Glu Gly Thr Leu Gln Arg Leu Pro Leu Ala Leu Thr Asn Trp Arg
                    85                  90                  95


    Ala Gln Gly Ser Gly Cys Gln Arg His Val Thr Arg Ala Lys Val Ser
                    100                 105                 110


    Ser Thr Glu Ala Val Ala Arg Asp Ala Ala Arg Ser Ile Arg Asn Asp
                115                 120                 125


    Trp Lys Val Gly Leu Asp Val Thr Pro Lys Pro Thr Ser Asn Val His
        130                 135                 140


    Val Ser Val Ala Gly Ser His Ser Gln Ala Ala Asn Phe Ala Ala Gln
    145                 150                 155                 160
```

Lys Thr His Gln Asp Gln Tyr Ser Phe Ser Thr Asp Thr Val Glu Cys
            165   170   175

Arg Phe Tyr Ser Phe His Val Val His Thr Pro Pro Leu His Pro Asp
        180   185   190

Phe Lys Arg Ala Leu Gly Asp Leu Pro His His Phe Asn Ala Ser Thr
        195   200   205

Gln Pro Ala Tyr Leu Arg Leu Ile Ser Asn Tyr Gly Thr His Phe Ile
    210   215   220

Arg Ala Val Glu Leu Gly Gly Arg Ile Ser Ala Leu Thr Ala Leu Arg
225   230   235   240

Thr Cys Glu Leu Ala Leu Glu Gly Leu Thr Asp Asn Glu Val Glu Asp
            245   250   255

Cys Leu Thr Val Glu Ala Gln Val Asn Ile Gly Ile His Gly Ser Ile
            260   265   270

Ser Ala Glu Ala Lys Ala Cys Glu Glu Lys Lys Lys His Lys Met
        275   280   285

Thr Ala Ser Phe His Gln Thr Tyr Arg Glu Arg His Ser Glu Val Val
    290   295   300

Gly Gly His His Thr Ser Ile Asn Asp Leu Leu Phe Gly Ile Gln Ala
305   310   315   320

Gly Pro Glu Gln Tyr Ser Ala Trp Val Asn Ser Val Pro Gly Ser Pro
            325   330   335

Gly Leu Val Asp Tyr Thr Leu Glu Pro Leu His Val Leu Leu Asp Ser
        340   345   350

Gln Asp Pro Arg Arg Glu Ala Leu Arg Arg Ala Leu Ser Gln Tyr Leu
        355   360   365

Thr Asp Arg Ala Arg Trp Arg Asp Cys Ser Arg Pro Cys Pro Pro Gly
    370   375   380

Arg Gln Lys Ser Pro Arg Asp Pro Cys Gln Cys Val Cys His Gly Ser
385   390   395   400

818

```
Ala Val Thr Thr Gln Asp Cys Cys Pro Arg Gln Arg Gly Leu Ala Gln
              405                 410                 415


Leu Glu Val Thr Phe Ile Gln Ala Trp Ser Leu Trp Gly Asp Trp Phe
              420                 425                 430


Thr Ala Thr Asp Ala Tyr Val Lys Leu Phe Phe Gly Gly Gln Glu Leu
          435                 440                 445


Arg Thr Ser Thr Val Trp Asp Asn Asn Asn Pro Ile Trp Ser Val Arg
    450                 455                 460


Leu Asp Phe Gly Asp Val Leu Leu Ala Thr Gly Gly Pro Leu Arg Leu
465                 470                 475                 480


Gln Val Trp Asp Gln Asp Ser Gly Arg Asp Asp Leu Leu Gly Thr
              485                 490                 495


Cys Asp Gln Ala Pro Lys Ser Gly Ser His Glu Val Arg Cys Asn Leu
          500                 505                 510


Asn His Gly His Leu Lys Phe Arg Tyr His Ala Arg Cys Leu Pro His
          515                 520                 525


Leu Gly Gly Gly Thr Cys Leu Asp Tyr Val Pro Gln Met Leu Leu Gly
    530                 535                 540


Glu Pro Pro Gly Asn Arg Ser Gly Ala Val Trp
545                 550                 555
```

```
<210>  2476
<211>  153
<212>  PRT
<213>  Homo sapiens

<400>  2476
```

```
Met Gly Leu Thr Ser Gln Leu Leu Pro Pro Leu Phe Phe Leu Leu Ala
1               5               10                  15


Cys Ala Gly Asn Phe Val His Gly His Lys Cys Asp Ile Thr Leu Gln
          20                  25                  30


Glu Ile Ile Lys Thr Leu Asn Ser Leu Thr Glu Gln Lys Thr Leu Cys
          35                  40                  45


Thr Glu Leu Thr Val Thr Asp Ile Phe Ala Ala Ser Lys Asn Thr Thr
    50                  55                  60
```

Glu Lys Glu Thr Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Phe Tyr
65   70   75   80

Ser His His Glu Lys Asp Thr Arg Cys Leu Gly Ala Thr Ala Gln Gln
                85   90   95

Phe His Arg His Lys Gln Leu Ile Arg Phe Leu Lys Arg Leu Asp Arg
                100   105   110

Asn Leu Trp Gly Leu Ala Gly Leu Asn Ser Cys Pro Val Lys Glu Ala
            115   120   125

Asn Gln Ser Thr Leu Glu Asn Phe Leu Glu Arg Leu Lys Thr Ile Met
        130   135   140

Arg Glu Lys Tyr Ser Lys Cys Ser Ser
145   150

<210> 2477
<211> 146
<212> PRT
<213> Homo sapiens

<400> 2477

Met His Pro Leu Leu Asn Pro Leu Leu Leu Ala Leu Gly Leu Met Ala
1   5   10   15

Leu Leu Leu Thr Thr Val Ile Ala Leu Thr Cys Leu Gly Gly Phe Ala
            20   25   30

Ser Pro Gly Pro Val Pro Pro Ser Thr Ala Leu Arg Glu Leu Ile Glu
        35   40   45

Glu Leu Val Asn Ile Thr Gln Asn Gln Lys Ala Pro Leu Cys Asn Gly
    50   55   60

Ser Met Val Trp Ser Ile Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala
65   70   75   80

Leu Glu Ser Leu Ile Asn Val Ser Gly Cys Ser Ala Ile Glu Lys Thr
                85   90   95

Gln Arg Met Leu Ser Gly Phe Cys Pro His Lys Val Ser Ala Gly Gln
            100   105   110

820

Phe Ser Ser Leu His Val Arg Asp Thr Lys Ile Glu Val Ala Gln Phe
        115   120   125

Val Lys Asp Leu Leu Leu His Leu Lys Lys Leu Phe Arg Glu Gly Gln
    130   135   140

Phe Asn
145

<210> 2478
<211> 223
<212> PRT
<213> Homo sapiens

<400> 2478

Met Ala Cys Leu Gly Phe Gln Arg His Lys Ala Gln Leu Asn Leu Ala
1   5   10   15

Thr Arg Thr Trp Pro Cys Thr Leu Leu Phe Phe Leu Leu Phe Ile Pro
                20   25   30

Val Phe Cys Lys Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala
        35   40   45

Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly
    50   55   60

Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln
65   70   75   80

Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr
                85   90   95

Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val
            100   105   110

Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile
        115   120   125

Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr Tyr Leu Gly Ile Gly
    130   135   140

Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu Pro Cys Pro Asp Ser
145   150   155   160

Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser Ser Gly Leu Phe Phe
                165   170   175

```
Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser Lys Met Leu Lys Lys
            180                 185             190


Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys Met Pro Pro Thr Glu
            195                 200             205


Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe Ile Pro Ile Asn
    210                 215             220
```

<210> 2479
<211> 235
<212> PRT
<213> Homo sapiens

<400> 2479

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5               10              15


His Ala Ala Arg Pro Ser Gln Phe Arg Val Ser Pro Leu Asp Arg Thr
            20              25              30


Trp Asn Leu Gly Glu Thr Val Glu Leu Lys Cys Gln Val Leu Leu Ser
        35              40              45


Asn Pro Thr Ser Gly Cys Ser Trp Leu Phe Gln Pro Arg Gly Ala Ala
    50              55              60


Ala Ser Pro Thr Phe Leu Leu Tyr Leu Ser Gln Asn Lys Pro Lys Ala
65              70              75              80


Ala Glu Gly Leu Asp Thr Gln Arg Phe Ser Gly Lys Arg Leu Gly Asp
            85              90              95


Thr Phe Val Leu Thr Leu Ser Asp Phe Arg Arg Glu Asn Glu Gly Tyr
            100             105             110


Tyr Phe Cys Ser Ala Leu Ser Asn Ser Ile Met Tyr Phe Ser His Phe
        115             120             125


Val Pro Val Phe Leu Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg
    130             135             140


Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
145             150             155             160
```

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
              165   170   175

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
          180   185   190

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Asn His
          195   200   205

Arg Asn Arg Arg Arg Val Cys Lys Cys Pro Arg Pro Val Val Lys Ser
    210   215   220

Gly Asp Lys Pro Ser Leu Ser Ala Arg Tyr Val
225   230   235

<210> 2480
<211> 181
<212> PRT
<213> Homo sapiens

<400> 2480

Met Leu Leu Glu Pro Gly Arg Gly Cys Cys Ala Leu Ala Ile Leu Leu
1   5   10   15

Ala Ile Val Asp Ile Gln Ser Gly Gly Cys Ile Asn Ile Thr Ser Ser
          20   25   30

Ala Ser Gln Glu Gly Thr Arg Leu Asn Leu Ile Cys Thr Val Trp His
          35   40   45

Lys Lys Glu Glu Ala Glu Gly Phe Val Val Phe Leu Cys Lys Asp Arg
    50   55   60

Ser Gly Asp Cys Ser Pro Glu Thr Ser Leu Lys Gln Leu Arg Leu Lys
65   70   75   80

Arg Asp Pro Gly Ile Asp Gly Val Gly Glu Ile Ser Ser Gln Leu Met
              85   90   95

Phe Thr Ile Ser Gln Val Thr Pro Leu His Ser Gly Thr Tyr Gln Cys
          100   105   110

Cys Ala Arg Ser Gln Lys Ser Gly Ile Arg Leu Gln Gly His Phe Phe
          115   120   125

Ser Ile Leu Phe Thr Glu Thr Gly Asn Tyr Thr Val Thr Gly Leu Lys
    130   135   140

Gln Arg Gln His Leu Glu Phe Ser His Asn Glu Gly Thr Leu Ser Ser
145   150   155   160

Gly Phe Leu Gln Glu Lys Val Trp Val Met Leu Val Thr Ser Leu Val
                165   170   175

Ala Leu Gln Ala Leu
            180

<210> 2481
<211> 147
<212> PRT
<213> Homo sapiens

<400> 2481

Met Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Ala Leu Trp
1   5   10   15

Gly Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly Arg Leu
                20   25   30

Leu Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Glu Ser Phe Gly Asp
            35   40   45

Leu Ser Thr Pro Asp Ala Val Met Gly Asn Pro Lys Val Lys Ala His
        50   55   60

Gly Lys Lys Val Leu Gly Ala Phe Ser Asp Gly Leu Ala His Leu Asp
65   70   75   80

Asn Leu Lys Gly Thr Phe Ala Thr Leu Ser Glu Leu His Cys Asp Lys
                85   90   95

Leu His Val Asp Pro Glu Asn Phe Arg Leu Leu Gly Asn Val Leu Val
            100   105   110

Cys Val Leu Ala His His Phe Gly Lys Glu Phe Thr Pro Pro Val Gln
        115   120   125

Ala Ala Tyr Gln Lys Val Val Ala Gly Val Ala Asn Ala Leu Ala His
    130   135   140

Lys Tyr His
145

<210> 2482
<211> 259
<212> PRT
<213> Homo sapiens

<400> 2482

Met Ser Lys Tyr Lys Leu Ile Met Leu Arg His Gly Glu Gly Ala Trp
1   5   10   15

Asn Lys Glu Asn Arg Phe Cys Ser Trp Val Asp Gln Lys Leu Asn Ser
            20   25   30

Glu Gly Met Glu Glu Ala Arg Asn Cys Gly Lys Gln Leu Lys Ala Leu
        35   40   45

Asn Phe Glu Phe Asp Leu Val Phe Thr Ser Val Leu Asn Arg Ser Ile
        50   55   60

His Thr Ala Trp Leu Ile Leu Glu Glu Leu Gly Gln Glu Trp Val Pro
65   70   75   80

Val Glu Ser Ser Trp Arg Leu Asn Glu Arg His Tyr Gly Ala Leu Ile
                85   90   95

Gly Leu Asn Arg Glu Gln Met Ala Leu Asn His Gly Glu Glu Gln Val
            100   105   110

Arg Leu Trp Arg Arg Ser Tyr Asn Val Thr Pro Pro Pro Ile Glu Glu
        115   120   125

Ser His Pro Tyr Tyr Gln Glu Ile Tyr Asn Asp Arg Arg Tyr Lys Val
    130   135   140

Cys Asp Val Pro Leu Asp Gln Leu Pro Arg Ser Glu Ser Leu Lys Asp
145   150   155   160

Val Leu Glu Arg Leu Leu Pro Tyr Trp Asn Glu Arg Ile Ala Pro Glu
                165   170   175

Val Leu Arg Gly Lys Thr Ile Leu Ile Ser Ala His Gly Asn Ser Ser
            180   185   190

Arg Ala Leu Leu Lys His Leu Glu Gly Ile Ser Asp Glu Asp Ile Ile
        195   200   205

Asn Ile Thr Leu Pro Thr Gly Val Pro Ile Leu Leu Glu Leu Asp Glu
        210   215   220

Asn Leu Arg Ala Val Gly Pro His Gln Phe Leu Gly Asp Gln Glu Ala
225   230   235   240

Ile Gln Ala Ala Ile Lys Lys Val Glu Asp Gln Gly Lys Val Lys Gln
            245   250   255

Ala Lys Lys

<210> 2483
<211> 344
<212> PRT
<213> Homo sapiens

<400> 2483

Met Ser Ala Leu Ala Ala Arg Leu Leu Gln Pro Ala His Ser Cys Ser
1   5   10   15

Leu Arg Leu Arg Pro Phe His Leu Ala Ala Val Arg Asn Glu Ala Val
            20   25   30

Val Ile Ser Gly Arg Lys Leu Ala Gln Gln Ile Lys Gln Glu Val Arg
            35   40   45

Gln Glu Val Glu Glu Trp Val Ala Ser Gly Asn Lys Arg Pro His Leu
        50   55   60

Ser Val Ile Leu Val Gly Glu Asn Pro Ala Ser His Ser Tyr Val Leu
65   70   75   80

Asn Lys Thr Arg Ala Ala Ala Val Val Gly Ile Asn Ser Glu Thr Ile
            85   90   95

Met Lys Pro Ala Ser Ile Ser Glu Glu Glu Leu Leu Asn Leu Ile Asn
            100   105   110

Lys Leu Asn Asn Asp Asp Asn Val Asp Gly Leu Leu Val Gln Leu Pro
            115   120   125

Leu Pro Glu His Ile Asp Glu Arg Arg Ile Cys Asn Ala Val Ser Pro
        130   135   140

Asp Lys Asp Val Asp Gly Phe His Val Ile Asn Val Gly Arg Met Cys
145   150   155   160

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Leu Asp Gln Tyr Ser Met Leu Pro Ala Thr Pro Trp Gly Val Trp Glu
                165   170   175

Ile Ile Lys Arg Thr Gly Ile Pro Thr Leu Gly Lys Asn Val Val Val
            180   185   190

Ala Gly Arg Ser Lys Asn Val Gly Met Pro Ile Ala Met Leu Leu His
            195   200   205

Thr Asp Gly Ala His Glu Arg Pro Gly Gly Asp Ala Thr Val Thr Ile
        210   215   220

Ser His Arg Tyr Thr Pro Lys Glu Gln Leu Lys Lys His Thr Ile Leu
225   230   235   240

Ala Asp Ile Val Ile Ser Ala Ala Gly Ile Pro Asn Leu Ile Thr Ala
            245   250   255

Asp Met Ile Lys Glu Gly Ala Ala Val Ile Asp Val Gly Ile Asn Arg
            260   265   270

Val His Asp Pro Val Thr Ala Lys Pro Lys Leu Val Gly Asp Val Asp
        275   280   285

Phe Glu Gly Val Arg Gln Lys Ala Gly Tyr Ile Thr Pro Val Pro Gly
    290   295   300

Gly Val Gly Pro Met Thr Val Ala Met Leu Met Lys Asn Thr Ile Ile
305   310   315   320

Ala Ala Lys Lys Val Leu Arg Leu Glu Glu Arg Glu Val Leu Lys Ser
            325   330   335

Lys Glu Leu Gly Val Ala Thr Asn
            340

<210>   2484
<211>   808
<212>   PRT
<213>   Homo sapiens

<400>   2484

Met Ala Glu Leu Leu Ala Ser Ala Gly Ser Ala Cys Ser Trp Asp Phe
1   5   10   15

Pro Arg Ala Pro Pro Ser Phe Pro Pro Ala Ala Ser Arg Gly Gly
            20   25   30

```
Leu Gly Gly Thr Arg Ser Phe Arg Pro His Arg Gly Ala Glu Ser Pro
        35              40              45

Arg Pro Gly Arg Asp Arg Asp Gly Val Arg Val Pro Met Ala Ser Ser
    50              55              60

Arg Cys Pro Ala Pro Arg Gly Cys Arg Cys Leu Pro Gly Ala Ser Leu
65              70              75              80

Ala Trp Leu Gly Thr Val Leu Leu Leu Leu Ala Asp Trp Val Leu Leu
            85              90              95

Arg Thr Ala Leu Pro Arg Ile Phe Ser Leu Leu Val Pro Thr Ala Leu
            100             105             110

Pro Leu Leu Arg Val Trp Ala Val Gly Leu Ser Arg Trp Ala Val Leu
        115             120             125

Trp Leu Gly Ala Cys Gly Val Leu Arg Ala Thr Val Gly Ser Lys Ser
    130             135             140

Glu Asn Ala Gly Ala Gln Gly Trp Leu Ala Ala Leu Lys Pro Leu Ala
145             150             155             160

Ala Ala Leu Gly Leu Ala Leu Pro Gly Leu Ala Leu Phe Arg Glu Leu
            165             170             175

Ile Ser Trp Gly Ala Pro Gly Ser Ala Asp Ser Thr Arg Leu Leu His
            180             185             190

Trp Gly Ser His Pro Thr Ala Phe Val Val Ser Tyr Ala Ala Ala Leu
    195             200             205

Pro Ala Ala Ala Leu Trp His Lys Leu Gly Ser Leu Trp Val Pro Gly
    210             215             220

Gly Gln Gly Gly Ser Gly Asn Pro Val Arg Arg Leu Leu Gly Cys Leu
225             230             235             240

Gly Ser Glu Thr Arg Arg Leu Ser Leu Phe Leu Val Leu Val Val Leu
            245             250             255

Ser Ser Leu Gly Glu Met Ala Ile Pro Phe Phe Thr Gly Arg Leu Thr
            260             265             270
```

Asp Trp Ile Leu Gln Asp Gly Ser Ala Asp Thr Phe Thr Arg Asn Leu
        275   280   285

Thr Leu Met Ser Ile Leu Thr Ile Ala Ser Ala Val Leu Glu Phe Val
        290   295   300

Gly Asp Gly Ile Tyr Asn Asn Thr Met Gly His Val His Ser His Leu
305   310   315   320

Gln Gly Glu Val Phe Gly Ala Val Leu Arg Gln Glu Thr Glu Phe Phe
            325   330   335

Gln Gln Asn Gln Thr Gly Asn Ile Met Ser Arg Val Thr Glu Asp Thr
            340   345   350

Ser Thr Leu Ser Asp Ser Leu Ser Glu Asn Leu Ser Leu Phe Leu Trp
        355   360   365

Tyr Leu Val Arg Gly Leu Cys Leu Leu Gly Ile Met Leu Trp Gly Ser
    370   375   380

Val Ser Leu Thr Met Val Thr Leu Ile Thr Leu Pro Leu Leu Phe Leu
385   390   395   400

Leu Pro Lys Lys Val Gly Lys Trp Tyr Gln Leu Leu Glu Val Gln Val
            405   410   415

Arg Glu Ser Leu Ala Lys Ser Ser Gln Val Ala Ile Glu Ala Leu Ser
            420   425   430

Ala Met Pro Thr Val Arg Ser Phe Ala Asn Glu Glu Gly Glu Ala Gln
        435   440   445

Lys Phe Arg Glu Lys Leu Gln Glu Ile Lys Thr Leu Asn Gln Lys Glu
    450   455   460

Ala Val Ala Tyr Ala Val Asn Ser Trp Thr Thr Ser Ile Ser Gly Met
465   470   475   480

Leu Leu Lys Val Gly Ile Leu Tyr Ile Gly Gly Gln Leu Val Thr Ser
            485   490   495

Gly Ala Val Ser Ser Gly Asn Leu Val Thr Phe Val Leu Tyr Gln Met
            500   505   510

```
Gln Phe Thr Gln Ala Val Glu Val Leu Leu Ser Ile Tyr Pro Arg Val
        515             520              525

Gln Lys Ala Val Gly Ser Ser Glu Lys Ile Phe Glu Tyr Leu Asp Arg
    530             535              540

Thr Pro Arg Cys Pro Pro Ser Gly Leu Leu Thr Pro Leu His Leu Glu
545             550              555              560

Gly Leu Val Gln Phe Gln Asp Val Ser Phe Ala Tyr Pro Asn Arg Pro
                565              570              575

Asp Val Leu Val Leu Gln Gly Leu Thr Phe Thr Leu Arg Pro Gly Glu
            580              585              590

Val Thr Ala Leu Val Gly Pro Asn Gly Ser Gly Lys Ser Thr Val Ala
        595              600              605

Ala Leu Leu Gln Asn Leu Tyr Gln Pro Thr Gly Gly Gln Leu Leu Leu
    610              615              620

Asp Gly Lys Pro Leu Pro Gln Tyr Glu His Arg Tyr Leu His Arg Gln
625              630              635              640

Val Ala Ala Val Gly Gln Glu Pro Gln Val Phe Gly Arg Ser Leu Gln
            645              650              655

Glu Asn Ile Ala Tyr Gly Leu Thr Gln Lys Pro Thr Met Glu Glu Ile
            660              665              670

Thr Ala Ala Ala Val Lys Ser Gly Ala His Ser Phe Ile Ser Gly Leu
    675              680              685

Pro Gln Gly Tyr Asp Thr Glu Val Asp Glu Ala Gly Ser Gln Leu Ser
    690              695              700

Gly Gly Gln Arg Gln Ala Val Ala Leu Ala Arg Ala Leu Ile Arg Lys
705              710              715              720

Pro Cys Val Leu Ile Leu Asp Asp Ala Thr Ser Ala Leu Asp Ala Asn
                725              730              735

Ser Gln Leu Gln Val Glu Gln Leu Leu Tyr Glu Ser Pro Glu Arg Tyr
        740              745              750

Ser Arg Ser Val Leu Leu Ile Thr Gln His Leu Ser Leu Val Glu Gln
```

```
              755                    760                    765

    Ala Asp His Ile Leu Phe Leu Glu Gly Gly Ala Ile Arg Glu Gly Gly
        770                 775                 780


    Thr His Gln Gln Leu Met Glu Lys Lys Gly Cys Tyr Trp Ala Met Val
    785                 790                 795                 800


    Gln Ala Pro Ala Asp Ala Pro Glu
                    805
```

<210> 2485
<211> 453
<212> PRT
<213> Homo sapiens

<400> 2485

```
    Met Ala Arg Lys Val Val Ser Arg Lys Arg Lys Ala Pro Ala Ser Pro
    1               5                   10                  15


    Gly Ala Gly Ser Asp Ala Gln Gly Pro Gln Phe Gly Trp Asp His Ser
                20                  25                  30


    Leu His Lys Arg Lys Arg Leu Pro Pro Val Lys Arg Ser Leu Val Tyr
                35                  40                  45


    Tyr Leu Lys Asn Arg Glu Val Arg Leu Gln Asn Glu Thr Ser Tyr Ser
        50                  55                  60


    Arg Val Leu His Gly Tyr Ala Ala Gln Gln Leu Pro Ser Leu Leu Lys
    65                  70                  75                  80


    Glu Arg Glu Phe His Leu Gly Thr Leu Asn Lys Val Phe Ala Ser Gln
                    85                  90                  95


    Trp Leu Asn His Arg Gln Val Val Cys Gly Thr Lys Cys Asn Thr Leu
                100                 105                 110


    Phe Val Val Asp Val Gln Thr Ser Gln Ile Thr Lys Ile Pro Ile Leu
                115                 120                 125


    Lys Asp Arg Glu Pro Gly Gly Val Thr Gln Gln Gly Cys Gly Ile His
        130                 135                 140


    Ala Ile Glu Leu Asn Pro Ser Arg Thr Leu Leu Ala Thr Gly Gly Asp
    145                 150                 155                 160
```

—

```
Asn Pro Asn Ser Leu Ala Ile Tyr Arg Leu Pro Thr Leu Asp Pro Val
            165                 170             175


Cys Val Gly Asp Asp Gly His Lys Asp Trp Ile Phe Ser Ile Ala Trp
            180             185             190


Ile Ser Asp Thr Met Ala Val Ser Gly Ser Arg Asp Gly Ser Met Gly
        195                 200             205


Leu Trp Glu Val Thr Asp Asp Val Leu Thr Lys Ser Asp Ala Arg His
    210                 215             220


Asn Val Ser Arg Val Pro Val Tyr Ala His Ile Thr His Lys Ala Leu
225                 230             235             240


Lys Asp Ile Pro Lys Glu Asp Thr Asn Pro Asp Asn Cys Lys Val Arg
            245             250             255


Ala Leu Ala Phe Asn Asn Lys Asn Lys Glu Leu Gly Ala Val Ser Leu
            260             265             270


Asp Gly Tyr Phe His Leu Trp Lys Ala Glu Asn Thr Leu Ser Lys Leu
        275             280             285


Leu Ser Thr Lys Leu Pro Tyr Cys Arg Glu Asn Val Cys Leu Ala Tyr
    290             295             300


Gly Ser Glu Trp Ser Val Tyr Ala Val Gly Ser Gln Ala His Val Ser
305             310             315             320


Phe Leu Asp Pro Arg Gln Pro Ser Tyr Asn Val Lys Ser Val Cys Ser
            325             330             335


Arg Glu Arg Gly Ser Gly Ile Arg Ser Val Ser Phe Tyr Glu His Ile
            340             345             350


Ile Thr Val Gly Thr Gly Gln Gly Ser Leu Leu Phe Tyr Asp Ile Arg
        355             360             365


Ala Gln Arg Phe Leu Glu Glu Arg Leu Ser Ala Cys Tyr Gly Ser Lys
        370             375             380


Pro Arg Leu Ala Gly Glu Asn Leu Lys Leu Thr Thr Gly Lys Gly Trp
385             390             395             400
```

```
Leu Asn His Asp Glu Thr Trp Arg Asn Tyr Phe Ser Asp Ile Asp Phe
            405                 410                 415

Phe Pro Asn Ala Val Tyr Thr His Cys Tyr Asp Ser Ser Gly Thr Lys
            420                 425                 430

Leu Phe Val Ala Gly Gly Pro Leu Pro Ser Gly Leu His Gly Asn Tyr
        435                 440                 445

Ala Gly Leu Trp Ser
    450
```

```
<210>  2486
<211>  352
<212>  PRT
<213>  Homo sapiens

<400>  2486
```

```
Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1               5                   10                  15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
            20              25                  30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
        35              40                  45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
    50              55                  60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65                  70              75                  80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
            85                  90                  95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
            100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130                 135                 140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160
```

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
              165   170   175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
              180   185   190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
          195   200   205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
      210   215   220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225   230   235   240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
              245   250   255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
              260   265   270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
          275   280   285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
      290   295   300

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305   310   315   320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
              325   330   335

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
          340   345   350

<210> 2487
<211> 199
<212> PRT
<213> Homo sapiens

<400> 2487

Met Ser Ser Glu Asn Cys Phe Val Ala Glu Asn Ser Ser Leu His Pro
1   5   10   15

```
Glu Ser Gly Gln Glu Asn Asp Ala Thr Ser Pro His Phe Ser Thr Arg
            20              25              30


His Glu Gly Ser Phe Gln Val Pro Val Leu Cys Ala Val Met Asn Val
            35              40              45


Val Phe Ile Thr Ile Leu Ile Ile Ala Leu Ile Ala Leu Ser Val Gly
    50              55              60


Gln Tyr Asn Cys Pro Gly Gln Tyr Thr Phe Ser Met Pro Ser Asp Ser
65              70              75              80


His Val Ser Ser Cys Ser Glu Asp Trp Val Gly Tyr Gln Arg Lys Cys
            85              90              95


Tyr Phe Ile Ser Thr Val Lys Arg Ser Trp Thr Ser Ala Gln Asn Ala
            100             105             110


Cys Ser Glu His Gly Ala Thr Leu Ala Val Ile Asp Ser Glu Lys Asp
            115             120             125


Met Asn Phe Leu Lys Arg Tyr Ala Gly Arg Glu Glu His Trp Val Gly
    130             135             140


Leu Lys Lys Glu Pro Gly His Pro Trp Lys Trp Ser Asn Gly Lys Glu
145             150             155             160


Phe Asn Asn Trp Phe Asn Val Thr Gly Ser Asp Lys Cys Val Phe Leu
            165             170             175


Lys Asn Thr Glu Val Ser Ser Met Glu Cys Glu Lys Asn Leu Tyr Trp
            180             185             190


Ile Cys Asn Lys Pro Tyr Lys
            195


<210>   2488
<211>   91
<212>   PRT
<213>   Homo sapiens

<400>   2488

Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1               5               10              15


Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
            20              25              30
```

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```
Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
        35                  40              45


Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val Phe
    50                  55              60


Val Thr Arg Lys Asn Arg Gln Val Cys Ala Asn Pro Glu Lys Lys Trp
65                  70              75                  80


Val Arg Glu Tyr Ile Asn Ser Leu Glu Met Ser
            85                  90
```

```
<210>   2489
<211>   212
<212>   PRT
<213>   Homo sapiens

<400>   2489

Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1               5                  10                  15


Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Val Pro Pro
            20                  25                  30


Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr
        35                  40                  45


Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile
    50                  55                  60


Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser
65                  70                  75                  80


Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala
                85                  90                  95


Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu
            100                 105                 110


Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr
        115                 120                 125


Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln
    130                 135                 140
```

Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn
145   150   155   160

Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
                165   170   175

Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His
            180   185   190

Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala
            195   200   205

Leu Arg Gln Met
        210

<210> 2490
<211> 153
<212> PRT
<213> Homo sapiens

<400> 2490

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1   5   10   15

Val Thr Asn Ser Ala Pro Thr Ser Ser Thr Lys Lys Thr Gln Leu
            20   25   30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
        35   40   45   .

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
    50   55   60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65   70   75   80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
            85   90   95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
            100   105   110   .

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
        115   120   125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
    130   .   135   140

Cys Gln Ser Ile Ile Ser Thr Leu Thr
145   150

<210> 2491
<211> 231
<212> PRT
<213> Homo sapiens

<400> 2491

Met Gln Asp Glu Glu Arg Tyr Met Thr Leu Asn Val Gln Ser Lys Lys
1   5   10   15

Arg Ser Ser Ala Gln Thr Ser Gln Leu Thr Phe Lys Asp Tyr Ser Val
            20   25   30

Thr Leu His Trp Tyr Lys Ile Leu Leu Gly Ile Ser Gly Thr Val Asn
        35   40   45

Gly Ile Leu Thr Leu Thr Leu Ile Ser Leu Ile Leu Leu Val Ser Gln
        50   55   60

Gly Val Leu Leu Lys Cys Gln Lys Gly Ser Cys Ser Asn Ala Thr Gln
65   70   75   80

Tyr Glu Asp Thr Gly Asp Leu Lys Val Asn Asn Gly Thr Arg Arg Asn
            85   90   95

Ile Ser Asn Lys Asp Leu Cys Ala Ser Arg Ser Ala Asp Gln Thr Val
            100   105   110

Leu Cys Gln Ser Glu Trp Leu Lys Tyr Gln Gly Lys Cys Tyr Trp Phe
        115   120   125

Ser Asn Glu Met Lys Ser Trp Ser Asp Ser Tyr Val Tyr Cys Leu Glu
    130   135   140

Arg Lys Ser His Leu Leu Ile Ile His Asp Gln Leu Glu Met Ala Phe
145   150   155   160

Ile Gln Lys Asn Leu Arg Gln Leu Asn Tyr Val Trp Ile Gly Leu Asn
            165   170   175

Phe Thr Ser Leu Lys Met Thr Trp Thr Trp Val Asp Gly Ser Pro Ile
            180   185   190

Asp Ser Lys Ile Phe Phe Ile Lys Gly Pro Ala Lys Glu Asn Ser Cys
        195   200   205

Ala Ala Ile Lys Glu Ser Lys Ile Phe Ser Glu Thr Cys Ser Ser Val
        210   215   220

Phe Lys Trp Ile Cys Gln Tyr
225   230

`

<210> 2492
<211> 512
<212> PRT
<213> Homo sapiens

<400> 2492

Met Gly Cys Ile Lys Ser Lys Gly Lys Asp Ser Leu Ser Asp Asp Gly
1   5   10   15

Val Asp Leu Lys Thr Gln Pro Val Arg Asn Thr Glu Arg Thr Ile Tyr
        20   25   30

Val Arg Asp Pro Thr Ser Asn Lys Gln Gln Arg Pro Val Pro Glu Ser
        35   40   45

Gln Leu Leu Pro Gly Gln Arg Phe Gln Thr Lys Asp Pro Glu Glu Gln
        50   55   60

Gly Asp Ile Val Val Ala Leu Tyr Pro Tyr Asp Gly Ile His Pro Asp
65   70   75   80

Asp Leu Ser Phe Lys Lys Gly Glu Lys Met Lys Val Leu Glu Glu His
                85   90   95

Gly Glu Trp Trp Lys Ala Lys Ser Leu Leu Thr Lys Lys Glu Gly Phe
                100   105   110

Ile Pro Ser Asn Tyr Val Ala Lys Leu Asn Thr Leu Glu Thr Glu Glu
        115   120   125

Trp Phe Phe Lys Asp Ile Thr Arg Lys Asp Ala Glu Arg Gln Leu Leu
        130   135   140

Ala Pro Gly Asn Ser Ala Gly Ala Phe Leu Ile Arg Glu Ser Glu Thr
145   150   155   160

Leu Lys Gly Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Pro Val His
                165   170   175

```
Gly Asp Val Ile Lys His Tyr Lys Ile Arg Ser Leu Asp Asn Gly Gly
            180             185                 190


Tyr Tyr Ile Ser Pro Arg Ile Thr Phe Pro Cys Ile Ser Asp Met Ile
        195                 200                 205


Lys His Tyr Gln Lys Gln Ala Asp Gly Leu Cys Arg Arg Leu Glu Lys
    210                 215                 220


Ala Cys Ile Ser Pro Lys Pro Gln Lys Pro Trp Asp Lys Asp Ala Trp
225                 230                 235                 240


Glu Ile Pro Arg Glu Ser Ile Lys Leu Val Lys Arg Leu Gly Ala Gly
            245                 250                 255


Gln Phe Gly Glu Val Trp Met Gly Tyr Tyr Asn Asn Ser Thr Lys Val
            260                 265                 270


Ala Val Lys Thr Leu Lys Pro Gly Thr Met Ser Val Gln Ala Phe Leu
        275                 280                 285


Glu Glu Ala Asn Leu Met Lys Thr Leu Gln His Asp Lys Leu Val Arg
    290                 295                 300


Leu Tyr Ala Val Val Thr Arg Glu Glu Pro Ile Tyr Ile Ile Thr Glu
305                 310                 315                 320


Tyr Met Ala Lys Gly Ser Leu Leu Asp Phe Leu Lys Ser Asp Glu Gly
            325                 330                 335


Gly Lys Val Leu Leu Pro Lys Leu Ile Asp Phe Ser Ala Gln Ile Ala
            340                 345                 350


Glu Gly Met Ala Tyr Ile Glu Arg Lys Asn Tyr Ile His Arg Asp Leu
    355                 360                 365


Arg Ala Ala Asn Val Leu Val Ser Glu Ser Leu Met Cys Lys Ile Ala
    370                 375                 380


Asp Phe Gly Leu Ala Arg Val Ile Glu Asp Asn Glu Tyr Thr Ala Arg
385                 390                 395                 400


Glu Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn
            405                 410                 415
```

```
Phe Gly Cys Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu
        420                 425                 430

Leu Tyr Glu Ile Val Thr Tyr Gly Lys Ile Pro Tyr Pro Gly Arg Thr
        435                 440                 445

Asn Ala Asp Val Met Thr Ala Leu Ser Gln Gly Tyr Arg Met Pro Arg
    450                 455                 460

Val Glu Asn Cys Pro Asp Glu Leu Tyr Asp Ile Met Lys Met Cys Trp
465                 470                 475                 480

Lys Glu Lys Ala Glu Glu Arg Pro Thr Phe Asp Tyr Leu Gln Ser Val
                485                 490                 495

Leu Asp Asp Phe Tyr Thr Ala Thr Glu Gly Gln Tyr Gln Gln Gln Pro
            500                 505                 510
```

```
<210>  2493
<211>  272
<212>  PRT
<213>  Homo sapiens

<400>  2493
```

```
Met Asp Ser Tyr Leu Leu Met Trp Gly Leu Leu Thr Phe Ile Met Val
1               5                   10                  15

Pro Gly Cys Gln Ala Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile Pro
            20                  25                  30

His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn
        35                  40                  45

Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr
    50                  55                  60

Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys
65                  70                  75                  80

Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro
                85                  90                  95

Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro
            100                 105                 110

Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro
```

115   120   125

Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val
        130   135   140

Gly Gln Met Val Tyr Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His
145   150   155   160

Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr Arg
                165   170   175

Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln
        180   185   190

Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu
        195   200   205

Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr
    210   215   220

Glu Met Ala Ala Thr Met Glu Thr Ser Ile Phe Thr Thr Glu Tyr Gln
225   230   235   240

Val Ala Val Ala Gly Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu
                245   250   255

Ser Gly Leu Thr Trp Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
        260   265   270

<210> 2494
<211> 92
<212> PRT
<213> Homo sapiens

<400> 2494

Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala
1   5   10   15

Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
            20   25   30

Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
            35   40   45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
    50   55   60

```
Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65                  70                  75                  80


Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
                85                  90
```

```
<210>   2495
<211>   532
<212>   PRT
<213>   Homo sapiens

<400>   2495
```

```
Met Met Met Val Arg Arg Gly Leu Leu Ala Trp Ile Ser Arg Val Val
1               5                   10                  15


Val Leu Leu Val Leu Leu Cys Cys Ala Ile Ser Val Leu Tyr Met Leu
            20                  25                  30


Ala Cys Thr Pro Lys Gly Asp Glu Glu Gln Leu Ala Leu Pro Arg Ala
            35                  40                  45


Asn Ser Pro Thr Gly Lys Glu Gly Tyr Gln Ala Val Leu Gln Glu Trp
        50                  55                  60


Glu Glu Gln His Arg Asn Tyr Val Ser Ser Leu Lys Arg Gln Ile Ala
65                  70                  75                  80


Gln Leu Lys Glu Glu Leu Gln Glu Arg Ser Glu Gln Leu Arg Asn Gly
                85                  90                  95


Gln Tyr Gln Ala Ser Asp Ala Ala Gly Leu Gly Leu Asp Arg Ser Pro
            100                 105                 110


Pro Glu Lys Thr Gln Ala Asp Leu Leu Ala Phe Leu His Ser Gln Val
        115                 120                 125


Asp Lys Ala Glu Val Asn Ala Gly Val Lys Leu Ala Thr Glu Tyr Ala
130                 135                 140


Ala Val Pro Phe Asp Ser Phe Thr Leu Gln Lys Val Tyr Gln Leu Glu
145                 150                 155                 160


Thr Gly Leu Thr Arg His Pro Glu Glu Lys Pro Val Arg Lys Asp Lys
                165                 170                 175


Arg Asp Glu Leu Val Glu Ala Ile Glu Ser Ala Leu Glu Thr Leu Asn
```

                    180   185   190

Asn Pro Ala Glu Asn Ser Pro Asn His Arg Pro Tyr Thr Ala Ser Asp
        195   200   205

Phe Ile Glu Gly Ile Tyr Arg Thr Glu Arg Asp Lys Gly Thr Leu Tyr
        210   215   220

Glu Leu Thr Phe Lys Gly Asp His Lys His Glu Phe Lys Arg Leu Ile
225   230   235   240

Leu Phe Arg Pro Phe Gly Pro Ile Met Lys Val Lys Asn Glu Lys Leu
                245   250   255

Asn Met Ala Asn Thr Leu Ile Asn Val Ile Val Pro Leu Ala Lys Arg
                260   265   270

Val Asp Lys Phe Arg Gln Phe Met Gln Asn Phe Arg Glu Met Cys Ile
        275   280   285

Glu Gln Asp Gly Arg Val His Leu Thr Val Val Tyr Phe Gly Lys Glu
        290   295   300

Glu Ile Asn Glu Val Lys Gly Ile Leu Glu Asn Thr Ser Lys Ala Ala
305   310   315   320

Asn Phe Arg Asn Phe Thr Phe Ile Gln Leu Asn Gly Glu Phe Ser Arg
                325   330   335

Gly Lys Gly Leu Asp Val Gly Ala Arg Phe Trp Lys Gly Ser Asn Val
                340   345   350

Leu Leu Phe Phe Cys Asp Val Asp Ile Tyr Phe Thr Ser Glu Phe Leu
                355   360   365

Asn Thr Cys Arg Leu Asn Thr Gln Pro Gly Lys Lys Val Phe Tyr Pro
        370   375   380

Val Leu Phe Ser Gln Tyr Asn Pro Gly Ile Ile Tyr Gly His His Asp
385   390   395   400

Ala Val Pro Pro Leu Glu Gln Gln Leu Val Ile Lys Lys Glu Thr Gly
                405   410   415

Phe Trp Arg Asp Phe Gly Phe Gly Met Thr Cys Gln Tyr Arg Ser Asp
                420   425   430

```
Phe Ile Asn Ile Gly Gly Phe Asp Leu Asp Ile Lys Gly Trp Gly Gly
        435             440             445


Glu Asp Val His Leu Tyr Arg Lys Tyr Leu His Ser Asn Leu Ile Val
    450             455             460


Val Arg Thr Pro Val Arg Gly Leu Phe His Leu Trp His Glu Lys Arg
465             470             475             480


Cys Met Asp Glu Leu Thr Pro Glu Gln Tyr Lys Met Cys Met Gln Ser
            485             490             495


Lys Ala Met Asn Glu Ala Ser His Gly Gln Leu Gly Met Leu Val Phe
            500             505             510


Arg His Glu Ile Glu Ala His Leu Arg Lys Gln Lys Gln Lys Thr Ser
        515             520             525


Ser Lys Lys Thr
    530
```

```
<210> 2496
<211> 125
<212> PRT
<213> Homo sapiens

<400> 2496
```

```
Met Lys Lys Ser Gly Val Leu Phe Leu Leu Gly Ile Ile Leu Leu Val
1               5               10              15


Leu Ile Gly Val Gln Gly Thr Pro Val Val Arg Lys Gly Arg Cys Ser
            20              25              30


Cys Ile Ser Thr Asn Gln Gly Thr Ile His Leu Gln Ser Leu Lys Asp
        35              40              45


Leu Lys Gln Phe Ala Pro Ser Pro Ser Cys Glu Lys Ile Glu Ile Ile
    50              55              60


Ala Thr Leu Lys Asn Gly Val Gln Thr Cys Leu Asn Pro Asp Ser Ala
65              70              75              80


Asp Val Lys Glu Leu Ile Lys Lys Trp Glu Lys Gln Val Ser Gln Lys
            85              90              95
```

```
Lys Lys Gln Lys Asn Gly Lys Lys His Gln Lys Lys Lys Val Leu Lys
            100                 105                 110

Val Arg Lys Ser Gln Arg Ser Arg Gln Lys Lys Thr Thr
            115                 120                 125
```

<210> 2497
<211> 98
<212> PRT
<213> Homo sapiens

<400> 2497

```
Met Asn Gln Thr Ala Ile Leu Ile Cys Cys Leu Ile Phe Leu Thr Leu
1               5                   10                  15

Ser Gly Ile Gln Gly Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys
            20                  25                  30

Ile Ser Ile Ser Asn Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu
            35                  40                  45

Glu Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala
    50                  55                  60

Thr Met Lys Lys Lys Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys
65                  70                  75                  80

Ala Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Met Ser Lys Arg
                85                  90                  95

Ser Pro
```

<210> 2498
<211> 155
<212> PRT
<213> Homo sapiens

<400> 2498

```
Met Thr Pro Gly Lys Thr Ser Leu Val Ser Leu Leu Leu Leu Leu Ser
1               5                   10                  15

Leu Glu Ala Ile Val Lys Ala Gly Ile Thr Ile Pro Arg Asn Pro Gly
            20                  25                  30

Cys Pro Asn Ser Glu Asp Lys Asn Phe Pro Arg Thr Val Met Val Asn
            35                  40                  45
```

```
Leu Asn Ile His Asn Arg Asn Thr Asn Thr Asn Pro Lys Arg Ser Ser
    50              55              60


Asp Tyr Tyr Asn Arg Ser Thr Ser Pro Trp Asn Leu His Arg Asn Glu
65              70              75              80


Asp Pro Glu Arg Tyr Pro Ser Val Ile Trp Glu Ala Lys Cys Arg His
'               85              90              95


Leu Gly Cys Ile Asn Ala Asp Gly Asn Val Asp Tyr His Met Asn Ser
            100             105             110


Val Pro Ile Gln Gln Glu Ile Leu Val Leu Arg Arg Glu Pro Pro His
        115             120             125


Cys Pro Asn Ser Phe Arg Leu Glu Lys Ile Leu Val Ser Val Gly Cys
    130             135             140


Thr Cys Val Thr Pro Ile Val His His Val Ala
145             150             155


<210>   2499
<211>   162
<212>   PRT
<213>   Homo sapiens

<400>   2499

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
1           5               10              15


Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His
        20              25              30


Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
        35              40              45


Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
    50              55              60


Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65              70              75              80


Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
            85              90              95


Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
```

```
              100                    105                    110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
          115                    120                    125


Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
      130                    135                    140


Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145                    150                    155                    160


Thr Ser



<210>   2500
<211>   178
<212>   PRT
<213>   Homo sapiens


<400>   2500

Met His Ser Ser Ala Leu Leu Cys Cys Leu Val Leu Leu Thr Gly Val
1                   5                   10                    15


Arg Ala Ser Pro Gly Gln Gly Thr Gln Ser Glu Asn Ser Cys Thr His
            20                    25                    30


Phe Pro Gly Asn Leu Pro Asn Met Leu Arg Asp Leu Arg Asp Ala Phe
            35                    40                    45


Ser Arg Val Lys Thr Phe Phe Gln Met Lys Asp Gln Leu Asp Asn Leu
      50                    55                    60


Leu Leu Lys Glu Ser Leu Leu Glu Asp Phe Lys Gly Tyr Leu Gly Cys
65                    70                    75                    80


Gln Ala Leu Ser Glu Met Ile Gln Phe Tyr Leu Glu Glu Val Met Pro
                85                    90                    95


Gln Ala Glu Asn Gln Asp Pro Asp Ile Lys Ala His Val Asn Ser Leu
            100                    105                    110


Gly Glu Asn Leu Lys Thr Leu Arg Leu Arg Leu Arg Arg Cys His Arg
            115                    120                    125


Phe Leu Pro Cys Glu Asn Lys Ser Lys Ala Val Glu Gln Val Lys Asn
      130                    135                    140
```

Ala Phe Asn Lys Leu Gln Glu Lys Gly Ile Tyr Lys Ala Met Ser Glu
145   150   155   160

Phe Asp Ile Phe Ile Asn Tyr Ile Glu Ala Tyr Met Thr Met Lys Ile
               165   170   175

Arg Asn

<210> 2501
<211> 166
<212> PRT
<213> Homo sapiens

<400> 2501

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1   5   10   15

Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu
               20   25   30

Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
          35   40   45

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
          50   55   60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65   70   75   80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
               85   90   95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
               100   105   110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
          115   120   125

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
          130   135   140

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Gln
145   150   155   160

Gly Arg Arg Ala Ser Gln

165

```
<210>  2502
<211>  266
<212>  PRT
<213>  Homo sapiens

<400>  2502
```

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Thr Ala Leu Thr
1   5   10   15

Val Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
            20   25   30

Arg Pro Arg Phe Leu Trp Gln Leu Lys Phe Glu Cys His Phe Phe Asn
        35   40   45

Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Cys Ile Tyr Asn Gln Glu
    50   55   60

Glu Ser Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65   70   75   80

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu
                85   90   95

Leu Glu Gln Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
            100   105   110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Glu Pro Lys Val
        115   120   125

Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
    130   135   140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145   150   155   160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
                165   170   175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
            180   185   190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
        195   200   205

Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210   215   220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225   230   235   240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
                245   250   255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
                260   265

<210>   2503
<211>   210
<212>   PRT
<213>   Homo sapiens

<400>   2503

Met Arg Pro Arg Leu Trp Leu Leu Leu Ala Ala Gln Leu Thr Val Leu
1   5   10   15

His Gly Asn Ser Val Leu Gln Gln Thr Pro Ala Tyr Ile Lys Val Gln
                20   25   30

Thr Asn Lys Met Val Met Leu Ser Cys Glu Ala Lys Ile Ser Leu Ser
            35   40   45

Asn Met Arg Ile Tyr Trp Leu Arg Gln Arg Gln Ala Pro Ser Ser Asp
    50   55   60

Ser His His Glu Phe Leu Ala Leu Trp Asp Ser Ala Lys Gly Thr Ile
65   70   75   80

His Gly Glu Glu Val Glu Gln Glu Lys Ile Ala Val Phe Arg Asp Ala
                85   90   95

Ser Arg Phe Ile Leu Asn Leu Thr Ser Val Lys Pro Glu Asp Ser Gly
            100   105   110

Ile Tyr Phe Cys Met Ile Val Gly Ser Pro Glu Leu Thr Phe Gly Lys
        115   120   125

Gly Thr Gln Leu Ser Val Val Asp Phe Leu Pro Thr Thr Ala Gln Pro
    130   135   140

Thr Lys Lys Ser Thr Leu Lys Lys Arg Val Cys Arg Leu Pro Arg Pro

851

145   150   155   160

Glu Thr Gln Lys Gly Pro Leu Cys Ser Pro Ile Thr Leu Gly Leu Leu
            165   170   175

Val Ala Gly Val Leu Val Leu Leu Val Ser Leu Gly Val Ala Ile His
            180   185   190

Leu Cys Cys Arg Arg Arg Arg Ala Arg Leu Arg Phe Met Lys Gln Phe
            195   200   205

Tyr Lys
    210

<210> 2504
<211> 458
<212> PRT
<213> Homo sapiens

<400> 2504

Met Asn Arg Gly Val Pro Phe Arg His Leu Leu Leu Val Leu Gln Leu
1   5   10   15

Ala Leu Leu Pro Ala Ala Thr Gln Gly Lys Lys Val Val Leu Gly Lys
            20   25   30

Lys Gly Asp Thr Val Glu Leu Thr Cys Thr Ala Ser Gln Lys Lys Ser
            35   40   45

Ile Gln Phe His Trp Lys Asn Ser Asn Gln Ile Lys Ile Leu Gly Asn
    50   55   60

Gln Gly Ser Phe Leu Thr Lys Gly Pro Ser Lys Leu Asn Asp Arg Ala
65   70   75   80

Asp Ser Arg Arg Ser Leu Trp Asp Gln Gly Asn Phe Pro Leu Ile Ile
            85   90   95

Lys Asn Leu Lys Ile Glu Asp Ser Asp Thr Tyr Ile Cys Glu Val Glu
            100   105   110

Asp Gln Lys Glu Glu Val Gln Leu Leu Val Phe Gly Leu Thr Ala Asn
            115   120   125

Ser Asp Thr His Leu Leu Gln Gly Gln Ser Leu Thr Leu Thr Leu Glu
    130   135   140

Ser Pro Pro Gly Ser Ser Pro Ser Val Gln Cys Arg Ser Pro Arg Gly
145   150   155   160

Lys Asn Ile Gln Gly Gly Lys Thr Leu Ser Val Ser Gln Leu Glu Leu
                165   170   175

Gln Asp Ser Gly Thr Trp Thr Cys Thr Val Leu Gln Asn Gln Lys Lys
                180   185   190

Val Glu Phe Lys Ile Asp Ile Val Val Leu Ala Phe Gln Lys Ala Ser
            195   200   205

Ser Ile Val Tyr Lys Lys Glu Gly Glu Gln Val Glu Phe Ser Phe Pro
        210   215   220

Leu Ala Phe Thr Val Glu Lys Leu Thr Gly Ser Gly Glu Leu Trp Trp
225   230   235   240

Gln Ala Glu Arg Ala Ser Ser Ser Lys Ser Trp Ile Thr Phe Asp Leu
                245   250   255

Lys Asn Lys Glu Val Ser Val Lys Arg Val Thr Gln Asp Pro Lys Leu
                260   265   270

Gln Met Gly Lys Lys Leu Pro Leu His Leu Thr Leu Pro Gln Ala Leu
                275   280   285

Pro Gln Tyr Ala Gly Ser Gly Asn Leu Thr Leu Ala Leu Glu Ala Lys
        290   295   300

Thr Gly Lys Leu His Gln Glu Val Asn Leu Val Val Met Arg Ala Thr
305   310   315   320

Gln Leu Gln Lys Asn Leu Thr Cys Glu Val Trp Gly Pro Thr Ser Pro
                325   330   335

Lys Leu Met Leu Ser Leu Lys Leu Glu Asn Lys Glu Ala Lys Val Ser
                340   345   350

Lys Arg Glu Lys Ala Val Trp Val Leu Asn Pro Glu Ala Gly Met Trp
            355   360   365

Gln Cys Leu Leu Ser Asp Ser Gly Gln Val Leu Leu Glu Ser Asn Ile
        37.0   375   380

853

Lys Val Leu Pro Thr Trp Ser Thr Pro Val Gln Pro Met Ala Leu Ile
385   390   395   400

Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly Leu Gly Ile
                405   410   415

Phe Phe Cys Val Arg Cys Arg His Arg Arg Arg Gln Ala Glu Arg Met
                420   425   430

Ser Gln Ile Lys Arg Leu Leu Ser Glu Lys Lys Thr Cys Gln Cys Pro
                435   440   445

His Arg Phe Gln Lys Thr Cys Ser Pro Ile
        450   455

<210>   2505
<211>   368
<212>   PRT
<213>   Homo sapiens

<400>   2505

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1   5   10   15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
                20   25   30

Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
        35   40   45

Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
    50   55   60

Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65   70   75   80

Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
                85   90   95

Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
            100   105   110

Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
            115   120   125

Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
            130   135   140

```
Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145                 150                 155                 160


Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
                165                 170                 175


Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
            180                 185                 190


His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
        195                 200                 205


Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220


Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240


Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255


Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
            260                 265                 270


Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
            275                 280                 285


Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300


Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320


Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335


Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
            340                 345                 350


Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
        355                 360                 365
```

<210> 2506
<211> 107
<212> PRT

<213> Homo sapiens

<400> 2506

Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1   5   10   15

Arg Val Ala Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala
            20   25   30

Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
        35   40   45

Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser
    50   55   60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
65   70   75   80

Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile
            85   90   95

Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn
            100   105

<210> 2507
<211> 558
<212> PRT
<213> Homo sapiens

<400> 2507

Met Ala Ala Leu Thr Arg Asp Pro Gln Phe Gln Lys Leu Gln Gln Trp
1   5   10   15

Tyr Arg Glu His Arg Ser Glu Leu Asn Leu Arg Arg Leu Phe Asp Ala
            20   25   30

Asn Lys Asp Arg Phe Asn His Phe Ser Leu Thr Leu Asn Thr Asn His
        35   40   45

Gly His Ile Leu Val Asp Tyr Ser Lys Asn Leu Val Thr Glu Asp Val
    50   55   60

Met Arg Met Leu Val Asp Leu Ala Lys Ser Arg Gly Val Glu Ala Ala
65   70   75   80

Arg Glu Arg Met Phe Asn Gly Glu Lys Ile Asn Tyr Thr Glu Gly Arg
            85   90   95

```
Ala Val Leu His Val Ala Leu Arg Asn Arg Ser Asn Thr Pro Ile Leu
            100             105             110

Val Asp Gly Lys Asp Val Met Pro Glu Val Asn Lys Val Leu Asp Lys
            115             120             125

Met Lys Ser Phe Cys Gln Arg Val Arg Ser Gly Asp Trp Lys Gly Tyr
            130             135             140

Thr Gly Lys Thr Ile Thr Asp Val Ile Asn Ile Gly Ile Gly Gly Ser
145             150             155             160

Asp Leu Gly Pro Leu Met Val Thr Glu Ala Leu Lys Pro Tyr Ser Ser
                165             170             175

Gly Gly Pro Arg Val Trp Tyr Val Ser Asn Ile Asp Gly Thr His Ile
                180             185             190

Ala Lys Thr Leu Ala Gln Leu Asn Pro Glu Ser Ser Leu Phe Ile Ile
            195             200             205

Ala Ser Lys Thr Phe Thr Thr Gln Glu Thr Ile Thr Asn Ala Glu Thr
210             215             220

Ala Lys Glu Trp Phe Leu Gln Ala Ala Lys Asp Pro Ser Ala Val Ala
225             230             235             240

Lys His Phe Val Ala Leu Ser Thr Asn Thr Thr Lys Val Lys Glu Phe
                245             250             255

Gly Ile Asp Pro Gln Asn Met Phe Glu Phe Trp Asp Trp Val Gly Gly
            260             265             270

Arg Tyr Ser Leu Trp Ser Ala Ile Gly Leu Ser Ile Ala Leu His Val
            275             280             285

Gly Phe Asp Asn Phe Glu Gln Leu Leu Ser Gly Ala His Trp Met Asp
    290             295             300

Gln His Phe Arg Thr Thr Pro Leu Glu Lys Asn Ala Pro Val Leu Leu
305             310             315             320

Ala Leu Leu Gly Ile Trp Tyr Ile Asn Cys Phe Gly Cys Glu Thr His
                325             330             335
```

Ala Met Leu Pro Tyr Asp Gln Tyr Leu His Arg Phe Ala Ala Tyr Phe
            340   345   350

Gln Gln Gly Asp Met Glu Ser Asn Gly Lys Tyr Ile Thr Lys Ser Gly
            355   360   365

Thr Arg Val Asp His Gln Thr Gly Pro Ile Val Trp Gly Glu Pro Gly
    370   375   380

Thr Asn Gly Gln His Ala Phe Tyr Gln Leu Ile His Gln Gly Thr Lys
385   390   395   400

Met Ile Pro Cys Asp Phe Leu Ile Pro Val Gln Thr Gln His Pro Ile
            405   410   415

Arg Lys Gly Leu His His Lys Ile Leu Leu Ala Asn Phe Leu Ala Gln
            420   425   430

Thr Glu Ala Leu Met Arg Gly Lys Ser Thr Glu Glu Ala Arg Lys Glu
            435   440   445

Leu Gln Ala Ala Gly Lys Ser Pro Glu Asp Leu Glu Arg Leu Leu Pro
    450   455   460

His Lys Val Phe Glu Gly Asn Arg Pro Thr Asn Ser Ile Val Phe Thr
465   470   475   480

Lys Leu Thr Pro Phe Met Leu Gly Ala Leu Val Ala Met Tyr Glu His
            485   490   495

Lys Ile Phe Val Gln Gly Ile Ile Trp Asp Ile Asn Ser Phe Asp Gln
            500   505   510

Trp Gly Val Glu Leu Gly Lys Gln Leu Ala Lys Lys Ile Glu Pro Glu
            515   520   525

Leu Asp Gly Ser Ala Gln Val Thr Ser His Asp Ala Ser Thr Asn Gly
    530   535   540

Leu Ile Asn Phe Ile Lys Gln Gln Arg Glu Ala Arg Val Gln
545   550   555

<210> 2508
<211> 323
<212> PRT
<213> Homo sapiens

858

<400> 2508

Met Trp Pro Leu Val Ala Ala Leu Leu Leu Gly Ser Ala Cys Cys Gly
1   5   10   15

Ser Ala Gln Leu Leu Phe Asn Lys Thr Lys Ser Val Glu Phe Thr Phe
                20   25   30

Cys Asn Asp Thr Val Val Ile Pro Cys Phe Val Thr Asn Met Glu Ala
            35   40   45

Gln Asn Thr Thr Glu Val Tyr Val Lys Trp Lys Phe Lys Gly Arg Asp
        50   55   60

Ile Tyr Thr Phe Asp Gly Ala Leu Asn Lys Ser Thr Val Pro Thr Asp
65   70   75   80

Phe Ser Ser Ala Lys Ile Glu Val Ser Gln Leu Leu Lys Gly Asp Ala
                85   90   95

Ser Leu Lys Met Asp Lys Ser Asp Ala Val Ser His Thr Gly Asn Tyr
                100   105   110

Thr Cys Glu Val Thr Glu Leu Thr Arg Glu Gly Glu Thr Ile Ile Glu
            115   120   125

Leu Lys Tyr Arg Val Val Ser Trp Phe Ser Pro Asn Glu Asn Ile Leu
        130   135   140

Ile Val Ile Phe Pro Ile Phe Ala Ile Leu Leu Phe Trp Gly Gln Phe
145   150   155   160

Gly Ile Lys Thr Leu Lys Tyr Arg Ser Gly Gly Met Asp Glu Lys Thr
                165   170   175

Ile Ala Leu Leu Val Ala Gly Leu Val Ile Thr Val Ile Val Ile Val
                180   185   190

Gly Ala Ile Leu Phe Val Pro Gly Glu Tyr Ser Leu Lys Asn Ala Thr
            195   200   205

Gly Leu Gly Leu Ile Val Thr Ser Thr Gly Ile Leu Ile Leu Leu His
    210   215   220

Tyr Tyr Val Phe Ser Thr Ala Ile Gly Leu Thr Ser Phe Val Ile Ala
225   230   235   240

```
Ile Leu Val Ile Gln Val Ile Ala Tyr Ile Leu Ala Val Val Gly Leu
             245             250             255

Ser Leu Cys Ile Ala Ala Cys Ile Pro Met His Gly Pro Leu Leu Ile
             260             265             270

Ser Gly Leu Ser Ile Leu Ala Leu Ala Gln Leu Leu Gly Leu Val Tyr
             275             280             285

Met Lys Phe Val Ala Ser Asn Gln Lys Thr Ile Gln Pro Pro Arg Lys
             290             295             300

Ala Val Glu Glu Pro Leu Asn Ala Phe Lys Glu Ser Lys Gly Met Met
305             310             315             320

Asn Asp Glu
```

```
<210>   2509
<211>   362
<212>   PRT
<213>   Homo sapiens

<400>   2509
```

```
Met Ala Pro Arg Ser Leu Leu Leu Leu Ser Gly Ala Leu Ala Leu
1               5               10              15

Thr Asp Thr Trp Ala Gly Ser His Ser Leu Arg Tyr Phe Ser Thr Ala
             20              25              30

Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Tyr Ile Ala Val Glu Tyr
             35              40              45

Val Asp Asp Thr Gln Phe Leu Arg Phe Asp Ser Asp Ala Ala Ile Pro
    50              55              60

Arg Met Glu Pro Arg Glu Pro Trp Val Glu Gln Glu Gly Pro Gln Tyr
65              70              75              80

Trp Glu Trp Thr Thr Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp Arg
             85              90              95

Val Ala Leu Arg Asn Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala Gly
             100             105             110
```

```
Ser His Thr Leu Gln Gly Met Asn Gly Cys Asp Met Gly Pro Asp Gly
        115                 120                 125


Arg Leu Leu Arg Gly Tyr His Gln His Ala Tyr Asp Gly Lys Asp Tyr
    130                 135                 140


Ile Ser Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Val
145                 150                 155                 160


Ala Gln Ile Thr Gln Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu Glu
                165                 170                 175


Phe Arg Thr Tyr Leu Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg Tyr
            180                 185                 190


Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Ala
        195                 200                 205


His Val Ala His His Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys
    210                 215                 220


Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg
225                 230                 235                 240


Asp Gly Glu Glu Gln Thr Gln Asp Thr Glu Leu Val Glu Thr Arg Pro
            245                 250                 255


Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro Ser
            260                 265                 270


Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu Pro
        275                 280                 285


Gln Pro Leu Ile Leu Arg Trp Glu Gln Ser Pro Gln Pro Thr Ile Pro
    290                 295                 300


Ile Val Gly Ile Val Ala Gly Leu Val Val Leu Gly Ala Val Val Thr
305                 310                 315                 320


Gly Ala Val Val Ala Ala Val Met Trp Arg Lys Lys Ser Ser Asp Arg
                325                 330                 335


Asn Arg Gly Ser Tyr Ser Gln Ala Ala Val Thr Asp Ser Ala Gln Gly
            340                 345                 350


Ser Gly Val Ser Leu Thr Ala Asn Lys Val
```

```
355                    360


Met Leu Ala Arg Ala Leu Leu Leu Cys Ala Val Leu Ala Leu Ser His
1               5                   10                  15


Thr Ala Asn Pro Cys Cys Ser His Pro Cys Gln Asn Arg Gly Val Cys
            20                  25                  30


Met Ser Val Gly Phe Asp Gln Tyr Lys Cys Asp Cys Thr Arg Thr Gly
        35                  40                  45


Phe Tyr Gly Glu Asn Cys Ser Thr Pro Glu Phe Leu Thr Arg Ile Lys
    50                  55                  60


Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His
65                  70                  75                  80


Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn
                85                  90                  95


Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser
            100                 105                 110


Pro Pro Thr Tyr Asn Ala Asp Tyr Gly Tyr Lys Ser Trp Glu Ala Phe
        115                 120                 125


Ser Asn Leu Ser Tyr Tyr Thr Arg Ala Leu Pro Pro Val Pro Asp Asp
    130                 135                 140


Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser
145                 150                 155                 160


Asn Glu Ile Val Glu Lys Leu Leu Leu Arg Arg Lys Phe Ile Pro Asp
                165                 170                 175


Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr
            180                 185                 190


His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn
        195                 200                 205
```

Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu
    210   215   220

Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr
225   230   235   240

Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln
            245   ·   250   255

Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala
            260   265   270

Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala
            275   280   285

Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln
    290   295   300

Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu
305   310   315   320

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln
            325   330   335

His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu
            340   345   350

Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn
    355   360   365

Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His
370   375   380

Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu
385   390   395   400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile
            405   410   415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys
            420   425   430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser
    435   440   445

863

Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe
    450   455   460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu
465   470   475   480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu
            485   490   495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly
            500   505   510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro
            515   520   525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile
            530   535   540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly
545   550   555   560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr
                565   570   575

Val Thr Ile Asn Ala Ser Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn
            580   585   590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu
        595   600

<210> 2511
<211> 343
<212> PRT
<213> Homo sapiens

<400> 2511

Met Pro Leu Cys Ser Leu Leu Thr Cys Leu Gly Leu Asn Val Leu Phe
1   5   10   15

Leu Thr Leu Asn Glu Gly Ala Trp Tyr Ser Val Gly Ala Leu Met Ile
            20   25   30

Ser Val Pro Ala Leu Leu Gly Tyr Leu Gln Glu Val Cys Arg Ala Arg
        35   40   45

Leu Pro Asp Ser Glu Leu Met Arg Arg Lys Tyr His Ser Val Arg Gln
        50   55   60

```
Glu Asp Leu Gln Arg Val Arg Leu Ser Arg Pro Glu Ala Val Ala Glu
65              70              75              80

Val Lys Ser Phe Leu Ile Gln Leu Glu Ala Phe Leu Ser Arg Leu Cys
            85              90              95

Cys Thr Cys Glu Ala Ala Tyr Arg Val Leu His Trp Glu Asn Pro Val
        100             105             110

Val Ser Ser Gln Phe Tyr Gly Ala Leu Leu Gly Thr Val Cys Met Leu
        115             120             125

Tyr Leu Leu Pro Leu Cys Trp Val Leu Thr Leu Leu Asn Ser Thr Leu
    130             135             140

Phe Leu Gly Asn Val Glu Phe Phe Arg Val Val Ser Glu Tyr Arg Ala
145             150             155             160

Ser Leu Gln Gln Arg Met Asn Pro Lys Gln Glu Glu His Ala Phe Glu
            165             170             175

Ser Pro Pro Pro Pro Asp Val Gly Gly Lys Asp Gly Leu Met Asp Ser
        180             185             190

Thr Pro Ala Leu Thr Pro Thr Glu Asp Leu Thr Pro Gly Ser Val Glu
        195             200             205

Glu Ala Glu Glu Ala Glu Pro Asp Glu Glu Phe Lys Asp Ala Ile Glu
    210             215             220

Glu Thr His Leu Val Val Leu Glu Asp Asp Glu Gly Ala Pro Cys Pro
225             230             235             240

Ala Glu Asp Glu Leu Ala Leu Gln Asp Asn Gly Phe Leu Ser Lys Asn
            245             250             255

Glu Val Leu Arg Ser Lys Val Ser Arg Leu Thr Glu Arg Leu Arg Lys
            260             265             270

Arg Tyr Pro Thr Asn Asn Phe Gly Asn Cys Thr Gly Cys Ser Ala Thr
        275             280             285

Phe Ser Val Leu Lys Lys Arg Arg Ser Cys Ser Asn Cys Gly Asn Ser
        290             295             300
```

865

Phe Cys Ser Arg Cys Cys Ser Phe Lys Val Pro Lys Ser Ser Met Gly
305   310   315   320

Ala Thr Ala Pro Glu Ala Gln Arg Glu Thr Val Phe Val Cys Ala Ser
                325   330   335

Cys Asn Gln Thr Leu Ser Lys
            340

<210> 2512
<211> 789
<212> PRT
<213> Homo sapiens

<400> 2512

Met Lys Met Asp Met Glu Asp Ala Asp Met Thr Leu Trp Thr Glu Ala
1   5   10   15

Glu Phe Glu Glu Lys Cys Thr Tyr Ile Val Asn Asp His Pro Trp Asp
            20   25   30

Ser Gly Ala Asp Gly Gly Thr Ser Val Gln Ala Glu Ala Ser Leu Pro
        35   40   45

Arg Asn Leu Leu Phe Lys Tyr Ala Thr Asn Ser Glu Glu Val Ile Gly
    50   55   60

Val Met Ser Lys Glu Tyr Ile Pro Lys Gly Thr Arg Phe Gly Pro Leu
65   70   75   80

Ile Gly Glu Ile Tyr Thr Asn Asp Thr Val Pro Lys Asn Ala Asn Arg
                85   90   95

Lys Tyr Phe Trp Arg Ile Tyr Ser Arg Gly Glu Leu His His Phe Ile
            100   105   110

Asp Gly Phe Asn Glu Glu Lys Ser Asn Trp Met Arg Tyr Val Asn Pro
        115   120   125

Ala His Ser Pro Arg Glu Gln Asn Leu Ala Ala Cys Gln Asn Gly Met
    130   135   140

Asn Ile Tyr Phe Tyr Thr Ile Lys Pro Ile Pro Ala Asn Gln Glu Leu
145   150   155   160

Leu Val Trp Tyr Cys Arg Asp Phe Ala Glu Arg Leu His Tyr Pro Tyr

866

                    165   170   175

    Pro Gly Glu Leu Thr Met Met Asn Leu Thr Gln Thr Gln Ser Ser Leu
                180   185   190

    Lys Gln Pro Ser Thr Glu Lys Asn Glu Leu Cys Pro Lys Asn Val Pro
            195   200   205

    Lys Arg Glu Tyr Ser Val Lys Glu Ile Leu Lys Leu Asp Ser Asn Pro
        210   215   220

    Ser Lys Gly Lys Asp Leu Tyr Arg Ser Asn Ile Ser Pro Leu Thr Ser
    225   230   235   240

    Glu Lys Asp Leu Asp Asp Phe Arg Arg Arg Gly Ser Pro Glu Met Pro
                245   250   255

    Phe Tyr Pro Arg Val Val Tyr Pro Ile Arg Ala Pro Leu Pro Glu Asp
                260   265   270

    Phe Leu Lys Ala Ser Leu Ala Tyr Gly Ile Glu Arg Pro Thr Tyr Ile
            275   280   285

    Thr Arg Ser Pro Ile Pro Ser Ser Thr Thr Pro Ser Pro Ser Ala Arg
        290   295   300

    Ser Ser Pro Asp Gln Ser Leu Lys Ser Ser Ser Pro His Ser Ser Pro
    305   310   315   320

    Gly Asn Thr Val Ser Pro Val Gly Pro Gly Ser Gln Glu His Arg Asp
                325   330   335

    Ser Tyr Ala Tyr Leu Asn Ala Ser Tyr Gly Thr Glu Gly Leu Gly Ser
                340   345   350

    Tyr Pro Gly Tyr Ala Pro Leu Pro His Leu Pro Pro Ala Phe Ile Pro
            355   360   365

    Ser Tyr Asn Ala His Tyr Pro Lys Phe Leu Leu Pro Pro Tyr Gly Met
        370   375   380

    Asn Cys Asn Gly Leu Ser Ala Val Ser Ser Met Asn Gly Ile Asn Asn
    385   390   395   400

    Phe Gly Leu Phe Pro Arg Leu Cys Pro Val Tyr Ser Asn Leu Leu Gly
                405   410   415

```
    Gly Gly Ser Leu Pro His Pro Met Leu Asn Pro Thr Ser Leu Pro Ser
                420             425             430


    Ser Leu Pro Ser Asp Gly Ala Arg Arg Leu Leu Gln Pro Glu His Pro
                435             440             445


    Arg Glu Val Leu Val Pro Ala Pro His Ser Ala Phe Ser Phe Thr Gly
                450             455             460


    Ala Ala Ala Ser Met Lys Asp Lys Ala Cys Ser Pro Thr Ser Gly Ser
    465             470             475             480


    Pro Thr Ala Gly Thr Ala Ala Thr Ala Glu His Val Val Gln Pro Lys
                    485             490             495


    Ala Thr Ser Ala Ala Met Ala Ala Pro Ser Ser Asp Glu Ala Met Asn
                500             505             510


    Leu Ile Lys Asn Lys Arg Asn Met Thr Gly Tyr Lys Thr Leu Pro Tyr
                515             520             525


    Pro Leu Lys Lys Gln Asn Gly Lys Ile Lys Tyr Glu Cys Asn Val Cys
        530             535             540


    Ala Lys Thr Phe Gly Gln Leu Ser Asn Leu Lys Val His Leu Arg Val
    545             550             555             560


    His Ser Gly Glu Arg Pro Phe Lys Cys Gln Thr Cys Asn Lys Gly Phe
                    565             570             575


    Thr Gln Leu Ala His Leu Gln Lys His Tyr Leu Val His Thr Gly Glu
                580             585             590


    Lys Pro His Glu Cys Gln Val Cys His Lys Arg Phe Ser Ser Thr Ser
        595             600             605


    Asn Leu Lys Thr His Leu Arg Leu His Ser Gly Glu Lys Pro Tyr Gln
        610             615             620


    Cys Lys Val Cys Pro Ala Lys Phe Thr Gln Phe Val His Leu Lys Leu
    625             630             635             640


    His Lys Arg Leu His Thr Arg Glu Arg Pro His Lys Cys Ser Gln Cys
                    645             650             655
```

```
His Lys Asn Tyr Ile His Leu Cys Ser Leu Lys Val His Leu Lys Gly
            660                 665                 670

Asn Cys Ala Ala Ala Pro Ala Pro Gly Leu Pro Leu Glu Asp Leu Thr
        675                 680                 685

Arg Ile Asn Glu Glu Ile Glu Lys Phe Asp Ile Ser Asp Asn Ala Asp
    690                 695                 700

Arg Leu Glu Asp Val Glu Asp Asp Ile Ser Val Ile Ser Val Val Glu
705                 710                 715                 720

Lys Glu Ile Leu Ala Val Val Arg Lys Glu Lys Glu Glu Thr Gly Leu
                725                 730                 735

Lys Val Ser Leu Gln Arg Asn Met Gly Asn Gly Leu Leu Ser Ser Gly
                740                 745                 750

Cys Ser Leu Tyr Glu Ser Ser Asp Leu Pro Leu Met Lys Leu Pro Pro
        755                 760                 765

Ser Asn Pro Leu Pro Leu Val Pro Val Lys Val Lys Gln Glu Thr Val
    770                 775                 780

Glu Pro Met Asp Pro
785
```

```
<210>  2513
<211>  381
<212>  PRT
<213>  Homo sapiens

<400>  2513
```

```
Met Pro Phe Ser Asn Ser His Asn Ala Leu Lys Leu Arg Phe Pro Ala
1               5                   10                  15

Glu Asp Glu Phe Pro Asp Leu Ser Ala His Asn Asn His Met Ala Lys
            20                  25                  30

Val Leu Thr Pro Glu Leu Tyr Ala Glu Leu Arg Ala Lys Ser Thr Pro
        35                  40                  45

Ser Gly Phe Thr Leu Asp Asp Val Ile Gln Thr Gly Val Asp Asn Pro
    50                  55                  60

Gly His Pro Tyr Ile Met Thr Val Gly Cys Val Ala Gly Asp Glu Glu
```

<pre>
   65   70   75   80

    Ser Tyr Glu Val Phe Lys Asp Leu Phe Asp Pro Ile Ile Glu Asp Arg
                     85   90   95

    His Gly Gly Tyr Lys Pro Ser Asp Glu His Lys Thr Asp Leu Asn Pro
                 100   105   110

   Asp Asn Leu Gln Gly Gly Asp Asp Leu Asp Pro Asn Tyr Val Leu Ser
               115   120   125

    Ser Arg Val Arg Thr Gly Arg Ser Ile Arg Gly Phe Cys Leu Pro Pro
                130   135   140

    His Cys Ser Arg Gly Glu Arg Arg Ala Ile Glu Lys Leu Ala Val Glu
    145   150   155   160

   Ala Leu Ser Ser Leu Asp Gly Asp Leu Ala Gly Arg Tyr Tyr Ala Leu
                   165   170   175

   Lys Ser Met Thr Glu Ala Glu Gln Gln Gln Leu Ile Asp Asp His Phe
                180   185   190

   Leu Phe Asp Lys Pro Val Ser Pro Leu Leu Leu Ala Ser Gly Met Ala
                195   200   205

    Arg Asp Trp Pro Asp Ala Arg Gly Ile Trp His Asn Asp Asn Lys Thr
    210   215   220

   Phe Leu Val Trp Val Asn Glu Glu Asp His Leu Arg Val Ile Ser Met
   225   230   235   240

    Gln Lys Gly Gly Asn Met Lys Glu Val Phe Thr Arg Phe Cys Thr Gly
                    245   250   255

    Leu Thr Gln Ile Glu Thr Leu Phe Lys Ser Lys Asp Tyr Glu Phe Met
                260   265   270

    Trp Asn Pro His Leu Gly Tyr Ile Leu Thr Cys Pro Ser Asn Leu Gly
                275   280   285

    Thr Gly Leu Arg Ala Gly Val His Ile Lys Leu Pro Asn Leu Gly Lys
        290   295   300

   His Glu Lys Phe Ser Glu Val Leu Lys Arg Leu Arg Leu Gln Lys Arg
   305   310   315   320
</pre>

Gly Thr Gly Gly Val Asp Thr Ala Ala Val Gly Gly Val Phe Asp Val
                    325   330   335

Ser Asn Ala Asp Arg Leu Gly Phe Ser Glu Val Glu Leu Val Gln Met
            340   345   350

Val Val Asp Gly Val Lys Leu Leu Ile Glu Met Glu Gln Arg Leu Glu
        355   360   365

Gln Gly Gln Ala Ile Asp Asp Leu Met Pro Ala Gln Lys
    370   375   380

<210>   2514
<211>   541
<212>   PRT
<213>   Homo sapiens

<400>   2514

Met Thr Thr Pro Ala Gly Ser Gly Ser Gly Phe Gly Ser Val Ser Trp
1   5   10   15

Trp Gly Leu Ser Pro Ala Leu Asp Leu Gln Ala Glu Ser Pro Pro Val
        20   25   30

Asp Pro Asp Ser Gln Ala Asp Thr Val His Ser Asn Pro Glu Leu Asp
        35   40   45

Val Leu Leu Leu Gly Ser Val Asp Gly Arg His Leu Leu Arg Thr Leu
    50   55   60

Ser Arg Ala Lys Phe Trp Pro Arg Arg Arg Phe Asn Phe Phe Val Leu
65   70   75   80

Glu Asn Asn Leu Glu Ala Val Ala Arg His Met Leu Ile Phe Ser Leu
            85   90   95

Ala Leu Glu Glu Pro Glu Lys Met Gly Leu Gln Glu Arg Ser Glu Thr
        100   105   110

Phe Leu Glu Val Trp Gly Asn Ala Leu Leu Arg Pro Pro Val Ala Ala
        115   120   125

Phe Val Arg Ala Gln Ala Asp Leu Leu Ala His Leu Val Pro Glu Pro
    130   135   140

871

Asp Arg Leu Glu Glu Gln Leu Pro Trp Leu Ser Leu Arg Ala Leu Lys
145   150   155   160

Phe Arg Glu Arg Asp Ala Leu Glu Ala Val Phe Arg Phe Trp Ala Gly
            165   170   175

Gly Glu Lys Gly Pro Gln Ala Phe Pro Met Ser Arg Leu Trp Asp Ser
            180   185   190

Arg Leu Arg His Tyr Leu Gly Ser Arg Tyr Asp Ala Arg Arg Gly Val
        195   200   205

Ser Asp Trp Asp Leu Arg Met Lys Leu His Asp Arg Gly Ala Gln Val
    210   215   220

Ile His Pro Gln Glu Phe Arg Arg Trp Arg Asp Thr Gly Val Ala Phe
225   230   235   240

Glu Leu Arg Asp Ser Ser Ala Tyr His Val Pro Asn Arg Thr Leu Ala
            245   250   255

Ser Gly Arg Leu Leu Ser Tyr Arg Gly Glu Arg Val Ala Ala Arg Gly
        260   265   270

Tyr Trp Gly Asp Ile Ala Thr Gly Pro Phe Val Ala Phe Gly Ile Glu
        275   280   285

Ala Asp Asp Glu Ser Leu Leu Arg Thr Ser Asn Gly Gln Pro Val Lys
    290   295   300

Thr Ala Gly Glu Ile Thr Gln His Asn Val Thr Glu Leu Leu Arg Asp
305   310   315   320

Val Ala Ala Trp Gly Arg Ala Arg Ala Thr Gly Gly Asp Leu Glu Glu
            325   330   335

Gln Gln His Ala Glu Gly Ser Pro Glu Pro Gly Thr Pro Ala Ala Pro
        340   345   350

Thr Pro Glu Ser Phe Thr Val His Phe Leu Pro Leu Asn Ser Ala Gln
        355   360   365

Thr Leu His His Lys Ser Cys Tyr Asn Gly Arg Phe Gln Leu Leu Tyr
    370   375   380

Val Ala Cys Gly Met Val His Leu Leu Ile Pro Glu Leu Gly Ala Cys

872

385   390   395   400

Val Ala Pro Gly Gly Asn Leu Ile Val Glu Leu Ala Arg Tyr Leu Val
                405   410   415

Asp Val Arg Gln Glu Gln Leu Gln Gly Phe Asn Thr Arg Val Arg Glu
            420   425   430

Leu Ala Gln Ala Ala Gly Phe Ala Pro Gln Thr Gly Ala Arg Pro Ser
            435   440   445

Glu Thr Phe Ala Arg Phe Cys Lys Ser Gln Glu Ser Ala Leu Gly Asn
    450   455   460

Thr Val Pro Ala Val Glu Pro Gly Thr Pro Pro Leu Asp Ile Leu Ala
465   470   475   480

Gln Pro Leu Glu Ala Ser Asn Pro Ala Leu Glu Gly Leu Thr Gln Pro
                485   490   495

Leu Gln Gly Gly Thr Pro His Cys Glu Pro Cys Gln Leu Pro Ser Glu
            500   505   510

Ser Pro Gly Ser Leu Ser Glu Val Leu Ala Gln Pro Gln Gly Ala Leu
            515   520   525

Ala Pro Pro Asn Cys Glu Ser Asp Ser Lys Thr Gly Val
    530   535   540

<210> 2515
<211> 288
<212> PRT
<213> Homo sapiens

<400> 2515

Met Ser Asp Ile Glu Glu Val Val Glu Glu Tyr Glu Glu Glu Glu Gln
1   5   10   15

Glu Glu Ala Ala Val Glu Glu Gln Glu Glu Ala Ala Glu Glu Asp Ala
            20   25   30

Glu Ala Glu Ala Glu Thr Glu Glu Thr Arg Ala Glu Glu Asp Glu Glu
            35   40   45

Glu Glu Glu Ala Lys Glu Ala Glu Asp Gly Pro Met Glu Glu Ser Lys
    50   55   60

```
Pro Lys Pro Arg Ser Phe Met Pro Asn Leu Val Pro Pro Lys Ile Pro
65              70              75              80

Asp Gly Glu Arg Val Asp Phe Asp Asp Ile His Arg Lys Arg Met Glu
            85              90              95

Lys Asp Leu Asn Glu Leu Gln Ala Leu Ile Glu Ala His Phe Glu Asn
            100             105             110

Arg Lys Lys Glu Glu Glu Glu Leu Val Ser Leu Lys Asp Arg Ile Glu
        115             120             125

Arg Arg Arg Ala Glu Arg Ala Glu Gln Gln Arg Ile Arg Asn Glu Arg
    130             135             140

Glu Lys Glu Arg Gln Asn Arg Leu Ala Glu Glu Arg Ala Arg Arg Glu
145             150             155             160

Glu Glu Glu Asn Arg Arg Lys Ala Glu Asp Glu Ala Arg Lys Lys Lys
            165             170             175

Ala Leu Ser Asn Met Met His Phe Gly Gly Tyr Ile Gln Lys Gln Ala
            180             185             190

Gln Thr Glu Arg Lys Ser Gly Lys Arg Gln Thr Glu Arg Glu Lys Lys
        195             200             205

Lys Lys Ile Leu Ala Glu Arg Arg Lys Val Leu Ala Ile Asp His Leu
    210             215             220

Asn Glu Asp Gln Leu Arg Glu Lys Ala Lys Glu Leu Trp Gln Ser Ile
225             230             235             240

Tyr Asn Leu Glu Ala Glu Lys Phe Asp Leu Gln Glu Lys Phe Lys Gln
            245             250             255

Gln Lys Tyr Glu Ile Asn Val Leu Arg Asn Arg Ile Asn Asp Asn Gln
            260             265             270

Lys Val Ser Lys Thr Arg Gly Lys Ala Lys Val Thr Gly Arg Trp Lys
    275             280             285
```

<210> 2516
<211> 154
<212> PRT
<213> Homo sapiens

874

<400>   2516

Met Gly Leu Ser Asp Gly Glu Trp Gln Leu Val Leu Asn Val Trp Gly
1   5   10   15

Lys Val Glu Ala Asp Ile Pro Gly His Gly Gln Glu Val Leu Ile Arg
            20   25   30

Leu Phe Lys Gly His Pro Glu Thr Leu Glu Lys Phe Asp Lys Phe Lys
        35   40   45

His Leu Lys Ser Glu Asp Glu Met Lys Ala Ser Glu Asp Leu Lys Lys
    50   55   60

His Gly Ala Thr Val Leu Thr Ala Leu Gly Gly Ile Leu Lys Lys Lys
65   70   75   80

Gly His His Glu Ala Glu Ile Lys Pro Leu Ala Gln Ser His Ala Thr
                85   90   95

Lys His Lys Ile Pro Val Lys Tyr Leu Glu Phe Ile Ser Glu Cys Ile
            100   105   110

Ile Gln Val Leu Gln Ser Lys His Pro Gly Asp Phe Gly Ala Asp Ala
        115   120   125

Gln Gly Ala Met Asn Lys Ala Leu Glu Leu Phe Arg Lys Asp Met Ala
    130   135   140

Ser Asn Tyr Lys Glu Leu Gly Phe Gln Gly
145   150

<210>   2517
<211>   501
<212>   PRT
<213>   Homo sapiens

<400>   2517

Met Val Arg Lys Pro Val Val Ser Thr Ile Ser Lys Gly Gly Tyr Leu
1   5   10   15

Gln Gly Asn Val Asn Gly Arg Leu Pro Ser Leu Gly Asn Lys Glu Pro
            20   25   30

Pro Gly Gln Glu Lys Val Gln Leu Lys Arg Lys Val Thr Leu Leu Arg
        35   40   45

```
Gly Val Ser Ile Ile Ile Gly Thr Ile Ile Gly Ala Gly Ile Phe Ile
    50              55              60

Ser Pro Lys Gly Val Leu Gln Asn Thr Gly Ser Val Gly Met Ser Leu
65              70              75              80

Thr Ile Trp Thr Val Cys Gly Val Leu Ser Leu Phe Gly Ala Leu Ser
            85              90              95

Tyr Ala Glu Leu Gly Thr Thr Ile Lys Lys Ser Gly Gly His Tyr Thr
            100             105             110

Tyr Ile Leu Glu Val Phe Gly Pro Leu Pro Ala Phe Val Arg Val Trp
        115             120             125

Val Glu Leu Leu Ile Ile Arg Pro Ala Ala Thr Ala Val Ile Ser Leu
    130             135             140

Ala Phe Gly Arg Tyr Ile Leu Glu Pro Phe Phe Ile Gln Cys Glu Ile
145             150             155             160

Pro Glu Leu Ala Ile Lys Leu Ile Thr Ala Val Gly Ile Thr Val Val
            165             170             175

Met Val Leu Asn Ser Met Ser Val Ser Trp Ser Ala Arg Ile Gln Ile
            180             185             190

Phe Leu Thr Phe Cys Lys Leu Thr Ala Ile Leu Ile Ile Ile Val Pro
        195             200             205

Gly Val Met Gln Leu Ile Lys Gly Gln Thr Gln Asn Phe Lys Asp Ala
    210             215             220

Phe Ser Gly Arg Asp Ser Ser Ile Thr Arg Leu Pro Leu Ala Phe Tyr
225             230             235             240

Tyr Gly Met Tyr Ala Tyr Ala Gly Trp Phe Tyr Leu Asn Phe Val Thr
            245             250             255

Glu Glu Val Glu Asn Pro Glu Lys Thr Ile Pro Leu Ala Ile Cys Ile
            260             265             270

Ser Met Ala Ile Val Thr Ile Gly Tyr Val Leu Thr Asn Val Ala Tyr
    275             280             285
```

876

```
Phe Thr Thr Ile Asn Ala Glu Glu Leu Leu Leu Ser Asn Ala Val Ala
    290             295             300

Val Thr Phe Ser Glu Arg Leu Leu Gly Asn Phe Ser Leu Ala Val Pro
305             310             315             320

Ile Phe Val Ala Leu Ser Cys Phe Gly Ser Met Asn Gly Gly Val Phe
            325             330             335

Ala Val Ser Arg Leu Phe Tyr Val Ala Ser Arg Glu Gly His Leu Pro
            340             345             350

Glu Ile Leu Ser Met Ile His Val Arg Lys His Thr Pro Leu Pro Ala
    355             360             365

Val Ile Val Leu His Pro Leu Thr Met Ile Met Leu Phe Ser Gly Asp
    370             375             380

Leu Asp Ser Leu Leu Asn Phe Leu Ser Phe Ala Arg Trp Leu Phe Ile
385             390             395             400

Gly Leu Ala Val Ala Gly Leu Ile Tyr Leu Arg Tyr Lys Cys Pro Asp
            405             410             415

Met His Arg Pro Phe Lys Val Pro Leu Phe Ile Pro Ala Leu Phe Ser
            420             425             430

Phe Thr Cys Leu Phe Met Val Ala Leu Ser Leu Tyr Ser Asp Pro Phe
        435             440             445

Ser Thr Gly Ile Gly Phe Val Ile Thr Leu Thr Gly Val Pro Ala Tyr
    450             455             460

Tyr Leu Phe Ile Ile Trp Asp Lys Lys Pro Arg Trp Phe Arg Ile Met
465             470             475             480

Ser Glu Lys Ile Thr Arg Thr Leu Gln Ile Ile Leu Glu Val Val Pro
            485             490             495

Glu Glu Asp Lys Leu
            500
```

```
<210>  2518
<211>  277
<212>  PRT
<213>  Homo sapiens
```

<400> 2518

```
Met Val Arg Leu Pro Leu Gln Cys Val Leu Trp Gly Cys Leu Leu Thr
1               5                   10                  15


Ala Val His Pro Glu Pro Pro Thr Ala Cys Arg Glu Lys Gln Tyr Leu
            20              25                  30


Ile Asn Ser Gln Cys Cys Ser Leu Cys Gln Pro Gly Gln Lys Leu Val
        35                  40                  45


Ser Asp Cys Thr Glu Phe Thr Glu Thr Glu Cys Leu Pro Cys Gly Glu
    50              55                  60


Ser Glu Phe Leu Asp Thr Trp Asn Arg Glu Thr His Cys His Gln His
65              70                  75                  80


Lys Tyr Cys Asp Pro Asn Leu Gly Leu Arg Val Gln Gln Lys Gly Thr
            85                  90                  95


Ser Glu Thr Asp Thr Ile Cys Thr Cys Glu Glu Gly Trp His Cys Thr
            100                 105                 110


Ser Glu Ala Cys Glu Ser Cys Val Leu His Arg Ser Cys Ser Pro Gly
        115                 120                 125


Phe Gly Val Lys Gln Ile Ala Thr Gly Val Ser Asp Thr Ile Cys Glu
    130                 135                 140


Pro Cys Pro Val Gly Phe Phe Ser Asn Val Ser Ser Ala Phe Glu Lys
145                 150                 155                 160


Cys His Pro Trp Thr Ser Cys Glu Thr Lys Asp Leu Val Val Gln Gln
                165                 170                 175


Ala Gly Thr Asn Lys Thr Asp Val Val Cys Gly Pro Gln Asp Arg Leu
            180                 185                 190


Arg Ala Leu Val Val Ile Pro Ile Ile Phe Gly Ile Leu Phe Ala Ile
    195                 200                 205


Leu Leu Val Leu Val Phe Ile Lys Lys Val Ala Lys Lys Pro Thr Asn
210                 215                 220


Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro Asp
225                 230                 235                 240
```

Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
            245   250   255

Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser
            260   265   270

Val Gln Glu Arg Gln
        275

<210> 2519
<211> 260
<212> PRT
<213> Homo sapiens

<400> 2519

Met Ala Arg Pro His Pro Trp Trp Leu Cys Val Leu Gly Thr Leu Val
1   5   10   15

Gly Leu Ser Ala Thr Pro Ala Pro Lys Ser Cys Pro Glu Arg His Tyr
            20   25   30

Trp Ala Gln Gly Lys Leu Cys Cys Gln Met Cys Glu Pro Gly Thr Phe
        35   40   45

Leu Val Lys Asp Cys Asp Gln His Arg Lys Ala Ala Gln Cys Asp Pro
    50   55   60

Cys Ile Pro Gly Val Ser Phe Ser Pro Asp His His Thr Arg Pro His
65   70   75   80

Cys Glu Ser Cys Arg His Cys Asn Ser Gly Leu Leu Val Arg Asn Cys
            85   90   95

Thr Ile Thr Ala Asn Ala Glu Cys Ala Cys Arg Asn Gly Trp Gln Cys
            100   105   110

Arg Asp Lys Glu Cys Thr Glu Cys Asp Pro Leu Pro Asn Pro Ser Leu
        115   120   125

Thr Ala Arg Ser Ser Gln Ala Leu Ser Pro His Pro Gln Pro Thr His
    130   135   140

Leu Pro Tyr Val Ser Glu Met Leu Glu Ala Arg Thr Ala Gly His Met
145   150   155   160

Gln Thr Leu Ala Asp Phe Arg Gln Leu Pro Ala Arg Thr Leu Ser Thr

```
                    165                      170                       175
```

```
    His Trp Pro Pro Gln Arg Ser Leu Cys Ser Ser Asp Phe Ile Arg Ile
                180                 185                 190
```

```
    Leu Val Ile Phe Ser Gly Met Phe Leu Val Phe Thr Leu Ala Gly Ala
                195                 200                 205
```

```
    Leu Phe Leu His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser
        210                 215                 220
```

```
    Pro Val Glu Pro Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu
    225                 230                 235                 240
```

```
    Glu Gly Ser Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro
                    245                 250                 255
```

```
    Ala Cys Ser Pro
                260
```

```
<210>  2520
<211>  329
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2520
```

```
Met Asp Pro Gln Cys Thr Met Gly Leu Ser Asn Ile Leu Phe Val Met
1               5               10                  15
```

```
Ala Phe Leu Leu Ser Gly Ala Ala Pro Leu Lys Ile Gln Ala Tyr Phe
            20                  25                  30
```

```
Asn Glu Thr Ala Asp Leu Pro Cys Gln Phe Ala Asn Ser Gln Asn Gln
        35                  40                  45
```

```
Ser Leu Ser Glu Leu Val Val Phe Trp Gln Asp Gln Glu Asn Leu Val
    50                  55                  60
```

```
Leu Asn Glu Val Tyr Leu Gly Lys Glu Lys Phe Asp Ser Val His Ser
65                  70                  75                  80
```

```
Lys Tyr Met Gly Arg Thr Ser Phe Asp Ser Asp Ser Trp Thr Leu Arg
                85                  90                  95
```

```
Leu His Asn Leu Gln Ile Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile
            100                 105                 110
```

```
His His Lys Lys Pro Thr Gly Met Ile Arg Ile His Gln Met Asn Ser
        115             120             125

Glu Leu Ser Val Leu Ala Asn Phe Ser Gln Pro Glu Ile Val Pro Ile
        130             135             140

Ser Asn Ile Thr Glu Asn Val Tyr Ile Asn Leu Thr Cys Ser Ser Ile
145             150             155             160

His Gly Tyr Pro Glu Pro Lys Lys Met Ser Val Leu Leu Arg Thr Lys
                165             170             175

Asn Ser Thr Ile Glu Tyr Asp Gly Ile Met Gln Lys Ser Gln Asp Asn
                180             185             190

Val Thr Glu Leu Tyr Asp Val Ser Ile Ser Leu Ser Val Ser Phe Pro
        195             200             205

Asp Val Thr Ser Asn Met Thr Ile Phe Cys Ile Leu Glu Thr Asp Lys
        210             215             220

Thr Arg Leu Leu Ser Ser Pro Phe Ser Ile Glu Leu Glu Asp Pro Gln
225             230             235             240

Pro Pro Pro Asp His Ile Pro Trp Ile Thr Ala Val Leu Pro Thr Val
                245             250             255

Ile Ile Cys Val Met Val Phe Cys Leu Ile Leu Trp Lys Trp Lys Lys
                260             265             270

Lys Lys Arg Pro Arg Asn Ser Tyr Lys Cys Gly Thr Asn Thr Met Glu
                275             280             285

Arg Glu Glu Ser Glu Gln Thr Lys Lys Arg Glu Lys Ile His Ile Pro
        290             295             300

Glu Arg Ser Asp Glu Ala Gln Arg Val Phe Lys Ser Ser Lys Thr Ser
305             310             315             320

Ser Cys Asp Lys Ser Asp Thr Cys Phe
                325
```

```
<210>  2521
<211>  132
<212>  PRT
<213>  Homo sapiens
```

<400> 2521

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1   5   10   15

Ile Cys Gly Gly Arg Val Val Cys Arg Pro Lys Lys Thr Glu Val Ser
            20   25   30

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
        35   40   45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
    50   55   60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65   70   75   80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
                85   90   95

Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
            100   105   110

Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
        115   120   125

Ile Leu Lys Met
        130

<210>   2522
<211>   491
<212>   PRT
<213>   Homo sapiens

<400>   2522

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1   5   10   15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
            20   25   30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
        35   40   45

Ser Leu Gly Asp Pro Leu Phe Pro Glu Leu Ala Glu Glu Ser Leu Lys
    50   55   60

```
Thr Phe Glu Gln Val Thr Glu Asp Cys Asn Glu Asn Pro Glu Lys Asp
65              70              75              80

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
            85              90              95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
            100             105             110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
            115             120             125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
    130             135             140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145             150             155             160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
            165             170             175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
            180             185             190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
    195             200             205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
    210             215             220

Thr Asn Gly Cys Ser Gln Ala Met Ala Ala Leu Gln Asn Leu Pro Gln
225             230             235             240

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
            245             250             255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
            260             265             270

Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
    275             280             285

Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
    290             295             300
```

```
Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305             310             315             320

Ser Val Met Leu Ala Lys Arg Pro Leu Ile Thr Lys Pro Glu Val Ile
                325             330             335

Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
                340             345             350

Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
        355             360             365

Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
    370             375             380

Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385             390             395             400

Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
            405             410             415

Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
            420             425             430

Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
        435             440             445

Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
    450             455             460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465             470             475             480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
                485             490
```

```
<210>   2523
<211>   491
<212>   PRT
<213>   Homo sapiens

<400>   2523

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1               5               10              15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
        20              25              30
```

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
    35   40   45

Ser Leu Gly Asp Pro Leu Phe Pro Glu Leu Ala Glu Glu Ser Leu Lys
    50   55   60

Thr Phe Glu Gln Val Thr Glu Asp Cys Asn Glu Asn Pro Glu Lys Asp
65   70   75   80

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
            85   90   95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
        100   105   110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
        115   120   125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
    130   135   140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145   150   155   160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
            165   170   175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
            180   185   190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
    195   200   205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
    210   215   220

Thr Asn Gly Cys Ser Gln Ala Met Ala Ala Leu Gln Asn Leu Pro Gln
225   230   235   240

Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
            245   250   255

Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
            260   265   270

885

```
Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
        275                 280                 285


Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
        290                 295                 300


Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305                 310                 315                 320


Ser Val Met Leu Ala Lys Arg Pro Leu Ile Thr Lys Pro Glu Val Ile
                325                 330                 335


Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
            340                 345                 350


Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
        355                 360                 365


Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
    370                 375                 380


Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385                 390                 395                 400


Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
            405                 410                 415


Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
        420                 425                 430


Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
        435                 440                 445


Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
    450                 455                 460


Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465                 470                 475                 480


His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
            485                 490
```

```
<210>  2524
<211>  641
<212>  PRT
<213>  Homo sapiens
```

<400> 2524

```
Met Ser Asp Glu Gly Pro Gly Thr Gly Pro Gly Asn Gly Leu Gly Glu
1               5                   10                  15

Lys Gly Asp Thr Ser Gly Pro Glu Gly Ser Gly Gly Ser Gly Pro Gln
            20                  25                  30

Arg Arg Gly Gly Asp Asn His Gly Arg Gly Arg Gly Arg Gly Arg Gly
        35                  40                  45

Arg Gly Gly Gly Arg Pro Gly Ala Pro Gly Gly Ser Gly Ser Gly Pro
    50                  55                  60

Arg His Arg Asp Gly Val Arg Arg Pro Gln Lys Arg Pro Ser Cys Ile
65                  70                  75                  80

Gly Cys Lys Gly Thr His Gly Gly Thr Gly Ala Gly Ala Gly Ala Gly
                85                  90                  95

Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
            100                 105                 110

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly
        115                 120                 125

Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala
    130                 135                 140

Gly Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly
145                 150                 155                 160

Gly Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly
            165                 170                 175

Ala Gly Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly
        180                 185                 190

Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly Gly Ala Gly
        195                 200                 205

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala
    210                 215                 220

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala
225                 230                 235                 240
```

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
                  245   250   255

Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly
              260   265   270

Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Gly Ala Gly
          275   280   285

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Ala Gly Gly Ala Gly
    290   295   300

Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Gly Gly Ala Gly Ala Gly
305   310   315   320

Gly Ala Gly Ala Gly Gly Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
          325   330   335

Arg Gly Arg Gly Gly Ser Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly
          340   345   350

Arg Arg Gly Arg Gly Arg Glu Arg Ala Arg Gly Gly Ser Arg Glu Arg
    355   360   365

Ala Arg Gly Arg Gly Arg Gly Arg Gly Glu Lys Arg Pro Arg Ser Pro
    370   375   380

Ser Ser Gln Ser Ser Ser Ser Gly Ser Pro Pro Arg Arg Pro Pro Pro
385   390   395   400

Gly Arg Arg Pro Phe Phe His Pro Val Gly Glu Ala Asp Tyr Phe Glu
              405   410   415

Tyr His Gln Glu Gly Gly Pro Asp Gly Glu Pro Asp Val Pro Pro Gly
          420   425   430

Ala Ile Glu Gln Gly Pro Ala Asp Asp Pro Gly Glu Gly Pro Ser Thr
    435   440   445

Gly Pro Arg Gly Gln Gly Asp Gly Gly Arg Arg Lys Lys Gly Gly Trp
450   455   460

Phe Gly Lys His Arg Gly Gln Gly Gly Ser Asn Pro Lys Phe Glu Asn
465   470   475   480

Ile Ala Glu Gly Leu Arg Ala Leu Leu Ala Arg Ser His Val Glu Arg
                485   490   495

Thr Thr Asp Glu Gly Thr Trp Val Ala Gly Val Phe Val Tyr Gly Gly
                500   505   510

Ser Lys Thr Ser Leu Tyr Asn Leu Arg Arg Gly Thr Ala Leu Ala Ile
                515   520   525

Pro Gln Cys Arg Leu Thr Pro Leu Ser Arg Leu Pro Phe Gly Met Ala
        530   535   540

Pro Gly Pro Gly Pro Gln Pro Gly Pro Leu Arg Glu Ser Ile Val Cys
545   550   555   560

Tyr Phe Met Val Phe Leu Gln Thr His Ile Phe Ala Glu Val Leu Lys
                565   570   575

Asp Ala Ile Lys Asp Leu Val Met Thr Lys Pro Ala Pro Thr Cys Asn
            580   585   590

Ile Arg Val Thr Val Cys Ser Phe Asp Asp Gly Val Asp Leu Pro Pro
        595   600   605

Trp Phe Pro Pro Met Val Glu Gly Ala Ala Ala Glu Gly Asp Asp Gly
    610   615   620

Asp Asp Gly Asp Glu Gly Gly Asp Gly Asp Glu Gly Glu Glu Gly Gln
625   630   635   640

Glu

<210> 2525
<211> 245
<212> PRT
<213> Homo sapiens

<400> 2525

Met Met Asp Pro Asn Ser Thr Ser Glu Asp Val Lys Phe Thr Pro Asp
1   5   10   15

Pro Tyr Gln Val Pro Phe Val Gln Ala Phe Asp Gln Ala Thr Arg Val
            20   25   30

Tyr Gln Asp Leu Gly Gly Pro Ser Gln Ala Pro Leu Pro Cys Val Leu

```
          35                    40                    45

Trp Pro Val Leu Pro Glu Pro Leu Pro Gln Gly Gln Leu Thr Ala Tyr
    50                  55                  60

His Val Ser Thr Ala Pro Thr Gly Ser Trp Phe Ser Ala Pro Gln Pro
65                  70                  75                  80

Ala Pro Glu Asn Ala Tyr Gln Ala Tyr Ala Ala Pro Gln Leu Phe Pro
                85                  90                  95

Val Ser Asp Ile Thr Gln Asn Gln Gln Thr Asn Gln Ala Gly Gly Glu
            100                 105                 110

Ala Pro Gln Pro Gly Asp Asn Ser Thr Val Gln Thr Ala Ala Ala Val
        115                 120                 125

Val Phe Ala Cys Pro Gly Ala Asn Gln Gly Gln Gln Leu Ala Asp Ile
    130                 135                 140

Gly Val Pro Gln Pro Ala Pro Val Ala Ala Pro Ala Arg Arg Thr Arg
145                 150                 155                 160

Lys Pro Gln Gln Pro Glu Ser Leu Glu Glu Cys Asp Ser Glu Leu Glu
                165                 170                 175

Ile Lys Arg Tyr Lys Asn Arg Val Ala Ser Arg Lys Cys Arg Ala Lys
            180                 185                 190

Phe Lys Gln Leu Leu Gln His Tyr Arg Glu Val Ala Ala Ala Lys Ser
        195                 200                 205

Ser Glu Asn Asp Arg Leu Arg Leu Leu Leu Lys Gln Met Cys Pro Ser
    210                 215                 220

Leu Asp Val Asp Ser Ile Ile Pro Arg Thr Pro Asp Val Leu His Glu
225                 230                 235                 240

Asp Leu Leu Asn Phe
                245


<210>  2526
<211>  491
<212>  PRT
<213>  Homo sapiens

<400>  2526
```

```
Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1               5               10              15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
            20              25              30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
        35              40              45

Ser Leu Gly Asp Pro Leu Phe Pro Glu Leu Ala Glu Glu Ser Leu Lys
    50              55              60

Thr Phe Glu Gln Val Thr Glu Asp Cys Asn Glu Asn Pro Glu Lys Asp
65              70              75              80

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
            85              90              95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
            100             105             110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
        115             120             125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
    130             135             140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145             150             155             160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
            165             170             175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
            180             185             190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
    195             200             205

Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
    210             215             220

Thr Asn Gly Cys Ser Gln Ala Met Ala Ala Leu Gln Asn Leu Pro Gln
225             230             235             240
```

891

```
Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
                245               250                   255


Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
                260               265                   270


Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
                275               280               285


Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
            290               295               300


Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305               310               315                   320


Ser Val Met Leu Ala Lys Arg Pro Leu Ile Thr Lys Pro Glu Val Ile
                325               330                   335


Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
                340               345               350


Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
            355               360               365


Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
            370               375               380


Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385               390               395                   400


Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
                405               410               415


Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
                420               425               430


Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
                435               440               445


Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
            450               455               460


Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465               470               475                   480


His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
```

485   490

```
<210>   2527
<211>   491
<212>   PRT
<213>   Homo sapiens

<400>   2527
```

Met Glu Ser Ser Ala Lys Arg Lys Met Asp Pro Asp Asn Pro Asp Glu
1   5   10   15

Gly Pro Ser Ser Lys Val Pro Arg Pro Glu Thr Pro Val Thr Lys Ala
            20   25   30

Thr Thr Phe Leu Gln Thr Met Leu Arg Lys Glu Val Asn Ser Gln Leu
        35   40   45

Ser Leu Gly Asp Pro Leu Phe Pro Glu Leu Ala Glu Glu Ser Leu Lys
    50   55   60

Thr Phe Glu Gln Val Thr Glu Asp Cys Asn Glu Asn Pro Glu Lys Asp
65   70   75   80

Val Leu Ala Glu Leu Val Lys Gln Ile Lys Val Arg Val Asp Met Val
                85   90   95

Arg His Arg Ile Lys Glu His Met Leu Lys Lys Tyr Thr Gln Thr Glu
            100   105   110

Glu Lys Phe Thr Gly Ala Phe Asn Met Met Gly Gly Cys Leu Gln Asn
        115   120   125

Ala Leu Asp Ile Leu Asp Lys Val His Glu Pro Phe Glu Glu Met Lys
    130   135   140

Cys Ile Gly Leu Thr Met Gln Ser Met Tyr Glu Asn Tyr Ile Val Pro
145   150   155   160

Glu Asp Lys Arg Glu Met Trp Met Ala Cys Ile Lys Glu Leu His Asp
                165   170   175

Val Ser Lys Gly Ala Ala Asn Lys Leu Gly Gly Ala Leu Gln Ala Lys
            180   185   190

Ala Arg Ala Lys Lys Asp Glu Leu Arg Arg Lys Met Met Tyr Met Cys
        195   200   205

```
Tyr Arg Asn Ile Glu Phe Phe Thr Lys Asn Ser Ala Phe Pro Lys Thr
210              215              220
```

```
Thr Asn Gly Cys Ser Gln Ala Met Ala Ala Leu Gln Asn Leu Pro Gln
225              230              235              240
```

```
Cys Ser Pro Asp Glu Ile Met Ala Tyr Ala Gln Lys Ile Phe Lys Ile
245              250              255
```

```
Leu Asp Glu Glu Arg Asp Lys Val Leu Thr His Ile Asp His Ile Phe
260              265              270
```

```
Met Asp Ile Leu Thr Thr Cys Val Glu Thr Met Cys Asn Glu Tyr Lys
275              280              285
```

```
Val Thr Ser Asp Ala Cys Met Met Thr Met Tyr Gly Gly Ile Ser Leu
290              295              300
```

```
Leu Ser Glu Phe Cys Arg Val Leu Cys Cys Tyr Val Leu Glu Glu Thr
305              310              315              320
```

```
Ser Val Met Leu Ala Lys Arg Pro Leu Ile Thr Lys Pro Glu Val Ile
325              330              335
```

```
Ser Val Met Lys Arg Arg Ile Glu Glu Ile Cys Met Lys Val Phe Ala
340              345              350
```

```
Gln Tyr Ile Leu Gly Ala Asp Pro Leu Arg Val Cys Ser Pro Ser Val
355              360              365
```

```
Asp Asp Leu Arg Ala Ile Ala Glu Glu Ser Asp Glu Glu Glu Ala Ile
370              375              380
```

```
Val Ala Tyr Thr Leu Ala Thr Ala Gly Val Ser Ser Ser Asp Ser Leu
385              390              395              400
```

```
Val Ser Pro Pro Glu Ser Pro Val Pro Ala Thr Ile Pro Leu Ser Ser
405              410              415
```

```
Val Ile Val Ala Glu Asn Ser Asp Gln Glu Glu Ser Glu Gln Ser Asp
420              425              430
```

```
Glu Glu Glu Glu Glu Gly Ala Gln Glu Glu Arg Glu Asp Thr Val Ser
435              440              445
```

894

```
Val Lys Ser Glu Pro Val Ser Glu Ile Glu Glu Val Ala Pro Glu Glu
    450             455             460

Glu Glu Asp Gly Ala Glu Glu Pro Thr Ala Ser Gly Gly Lys Ser Thr
465             470             475             480

His Pro Met Val Thr Arg Ser Lys Ala Asp Gln
                485             490
```

```
<210>   2528
<211>   142
<212>   PRT
<213>   Homo sapiens

<400>   2528
```

```
Met Ser Leu Leu Pro Val Pro Tyr Thr Glu Ala Ala Ser Leu Ser Thr
1               5               10              15

Gly Ser Thr Val Thr Ile Lys Gly Arg Pro Leu Ala Cys Phe Leu Asn
            20              25              30

Glu Pro Tyr Leu Gln Val Asp Phe His Thr Glu Met Lys Glu Glu Ser
        35              40              45

Asp Ile Val Phe His Phe Gln Val Cys Phe Gly Arg Arg Val Val Met
    50              55              60

Asn Ser Arg Glu Tyr Gly Ala Trp Lys Gln Gln Val Glu Ser Lys Asn
65              70              75              80

Met Pro Phe Gln Asp Gly Gln Glu Phe Glu Leu Ser Ile Ser Val Leu
            85              90              95

Pro Asp Lys Tyr Gln Val Met Val Asn Gly Gln Ser Ser Tyr Thr Phe
            100             105             110

Asp His Arg Ile Lys Pro Glu Ala Val Lys Met Val Gln Val Trp Arg
        115             120             125

Asp Ile Ser Leu Thr Lys Phe Asn Val Ser Tyr Leu Lys Arg
    130             135             140
```

```
<210>   2529
<211>   298
<212>   PRT
<213>   Homo sapiens

<400>   2529
```

```
Met Ala Glu Ala Met Asp Leu Gly Lys Asp Pro Asn Gly Pro Thr His
1               5                   10                  15


Ser Ser Thr Leu Phe Val Arg Asp Asp Gly Ser Ser Met Ser Phe Tyr
            20                  25                  30


Val Arg Pro Ser Pro Ala Lys Arg Arg Leu Ser Thr Leu Ile Leu His
        35                  40                  45


Gly Gly Gly Thr Val Cys Arg Val Gln Glu Pro Gly Ala Val Leu Leu
    50                  55                  60


Ala Gln Pro Gly Glu Ala Leu Ala Glu Ala Ser Gly Asp Phe Ile Ser
65                  70                  75                  80


Thr Gln His Ile Leu Asp Cys Val Glu Arg Asn Glu Arg Leu Glu Leu
                85                  90                  95


Glu Ala Tyr Arg Leu Gly Pro Ala Ser Ala Ala Asp Thr Gly Ser Glu
            100                 105                 110


Ala Lys Pro Gly Ala Leu Ala Glu Gly Ala Ala Glu Pro Glu Pro Gln
        115                 120                 125


Arg His Ala Gly Arg Ile Ala Phe Thr Asp Ala Asp Asp Val Ala Ile
    130                 135                 140


Leu Thr Tyr Val Lys Glu Asn Ala Arg Ser Pro Ser Ser Val Thr Gly
145                 150                 155                 160


Asn Ala Leu Trp Lys Ala Met Glu Lys Ser Ser Leu Thr Gln His Ser
                165                 170                 175


Trp Gln Ser Leu Lys Asp Arg Tyr Leu Lys His Leu Arg Gly Gln Glu
            180                 185                 190


His Lys Tyr Leu Leu Gly Asp Ala Pro Val Ser Pro Ser Ser Gln Lys
        195                 200                 205


Leu Lys Arg Lys Ala Glu Glu Asp Pro Glu Ala Ala Asp Ser Gly Glu
    210                 215                 220


Pro Gln Asn Lys Arg Thr Pro Asp Leu Pro Glu Glu Glu Tyr Val Lys
225                 230                 235                 240
```

Glu Glu Ile Gln Glu Asn Glu Glu Ala Val Lys Lys Met Leu Val Glu
                245   250   255

Ala Thr Arg Glu Phe Glu Glu Val Val Val Asp Glu Ser Pro Pro Asp
        260   265   270

Phe Glu Ile His Ile Thr Met Cys Asp Asp Asp Pro Pro Thr Pro Glu
        275   280   285

Glu Asp Ser Glu Thr Gln Pro Asp Glu Glu
    290   295

<210> 2530
<211> 365
<212> PRT
<213> Homo sapiens

<400> 2530

Met Ala Val Met Ala Pro Arg Thr Leu Leu Leu Leu Ser Gly Ala
1   5   10   15

Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
        20   25   30

Phe Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
        35   40   45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
    50   55   60

Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65   70   75   80

Pro Glu Tyr Trp Asp Gln Glu Thr Arg Asn Val Lys Ala Gln Ser Gln
            85   90   95

Thr Asp Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
        100   105   110

Glu Ala Gly Ser His Thr Ile Gln Ile Met Tyr Gly Cys Asp Val Gly
        115   120   125

Ser Asp Gly Arg Phe Leu Arg Gly Tyr Arg Gln Asp Ala Tyr Asp Gly
    130   135   140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145   150   155   160

Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Ala His Glu
                165   170   175

Ala Glu Gln Leu Arg Ala Tyr Leu Asp Gly Thr Cys Val Glu Trp Leu
                180   185   190

Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro
                195   200   205

Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210   215   220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225   230   235   240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
                245   250   255

Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
                260   265   270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
                275   280   285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Leu Ser Ser Gln Pro
    290   295   300

Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala
305   310   315   320

Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser
                325   330   335

Ser Asp Arg Lys Gly Gly Ser Tyr Thr Gln Ala Ala Ser Ser Asp Ser
                340   345   350

Ala Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val
                355   360   365

<210> 2531
<211> 155
<212> PRT
<213> Homo sapiens

<400> 2531

```
Met Glu Leu Arg Ser Gly Ser Val Gly Ser Gln Ala Val Ala Arg Arg
1               5                   10                  15

Met Asp Gly Asp Ser Arg Asp Gly Gly Gly Lys Asp Ala Thr Gly
        20                  25                  30

Ser Glu Asp Tyr Glu Asn Leu Pro Thr Ser Ala Ser Val Ser Thr His
        35                  40                  45

Met Thr Ala Gly Ala Met Ala Gly Ile Leu Glu His Ser Val Met Tyr
    50              55                  60

Pro Val Asp Ser Val Lys Thr Arg Met Gln Ser Leu Ser Pro Asp Pro
65                  70                  75                  80

Lys Ala Gln Tyr Thr Ser Ile Tyr Gly Ala Leu Lys Lys Ile Met Arg
                85                  90                  95

Thr Glu Gly Phe Trp Arg Pro Leu Arg Gly Val Asn Val Met Ile Met
            100                 105                 110

Gly Ala Gly Pro Ala His Ala Met Tyr Phe Ala Cys Tyr Glu Asn Met
        115                 120                 125

Lys Arg Thr Leu Asn Asp Val Phe His His Gln Gly Asn Ser His Leu
    130                 135                 140

Ala Asn Gly Ile Leu Lys Ala Phe Val Trp Ser
145                 150                 155
```

```
<210>  2532
<211>  384
<212>  PRT
<213>  Homo sapiens

<400>  2532
```

```
Met Lys Val Thr Ser Leu Asp Gly Arg Gln Leu Arg Lys Met Leu Arg
1               5                   10                  15

Lys Glu Ala Ala Ala Arg Cys Val Val Leu Asp Cys Arg Pro Tyr Leu
                20                  25                  30

Ala Phe Ala Ala Ser Asn Val Arg Gly Ser Leu Asn Val Asn Leu Asn
        35                  40                  45

Ser Val Val Leu Arg Arg Ala Arg Gly Gly Ala Val Ser Ala Arg Tyr
        50                  55                  60
```

```
Val Leu Pro Asp Glu Ala Ala Arg Ala Arg Leu Leu Gln Glu Gly Gly
65                   70                  75                  80

Gly Gly Val Ala Ala Val Val Val Leu Asp Gln Gly Ser Arg His Trp
                 85                  90                  95

Gln Lys Leu Arg Glu Glu Ser Ala Ala Arg Val Val Leu Thr Ser Leu
             100                 105                 110

Leu Ala Cys Leu Pro Ala Gly Pro Arg Val Tyr Phe Leu Lys Gly Gly
         115                 120                 125

Tyr Glu Thr Phe Tyr Ser Glu Tyr Pro Glu Cys Cys Val Asp Val Lys
    130                 135                 140

Pro Ile Ser Gln Glu Lys Ile Glu Ser Glu Arg Ala Leu Ile Ser Gln
145                 150                 155                 160

Cys Gly Lys Pro Val Val Asn Val Ser Tyr Arg Pro Ala Tyr Asp Gln
             165                 170                 175

Gly Gly Pro Val Glu Ile Leu Pro Phe Leu Tyr Leu Gly Ser Ala Tyr
         180                 185                 190

His Ala Ser Lys Cys Glu Phe Leu Ala Asn Leu His Ile Thr Ala Leu
    195                 200                 205

Leu Asn Val Ser Arg Arg Thr Ser Glu Ala Cys Met Thr His Leu His
210                 215                 220

Tyr Lys Trp Ile Pro Val Glu Asp Ser His Thr Ala Asp Ile Ser Ser
225                 230                 235                 240

His Phe Gln Glu Ala Ile Asp Phe Ile Asp Cys Val Arg Glu Lys Gly
             245                 250                 255

Gly Lys Val Leu Val His Cys Glu Ala Gly Ile Ser Arg Ser Pro Thr
         260                 265                 270

Ile Cys Met Ala Tyr Leu Met Lys Thr Lys Gln Phe Arg Leu Lys Glu
    275                 280                 285

Ala Phe Asp Tyr Ile Lys Gln Arg Arg Ser Met Val Ser Pro Asn Phe
290                 295                 300
```

```
Gly Phe Met Gly Gln Leu Leu Gln Tyr Glu Ser Glu Ile Leu Pro Ser
305             310             315             320


Thr Pro Asn Pro Gln Pro Pro Ser Cys Gln Gly Glu Ala Ala Gly Ser
                325             330             335


Ser Leu Ile Gly His Leu Gln Thr Leu Ser Pro Asp Met Gln Gly Ala
            340             345             350


Tyr Cys Thr Phe Pro Ala Ser Val Leu Ala Pro Val Pro Thr His Ser
        355             360             365


Thr Val Ser Glu Leu Ser Arg Ser Pro Val Ala Thr Ala Thr Ser Cys
    370             375             380
```

```
<210>  2533
<211>  99
<212>  PRT
<213>  Homo sapiens

<400>  2533
```

```
Met Ala Gln Gly Lys Val Ala Ser Leu Gly Pro Ile Lys Gln His Thr
1               5               10              15


Phe Leu Lys Asn Met Gly Ile Asp Val Arg Leu Lys Val Leu Leu Asp
            20              25              30


Lys Ser Asn Glu Pro Ser Val Arg Gln Gln Leu Leu Gln Gly Tyr Asp
        35              40              45


Met Leu Met Asn Pro Lys Lys Met Gly Glu Arg Phe Asn Phe Phe Ala
    50              55              60


Leu Leu Pro His Gln Arg Leu Gln Gly Gly Arg Tyr Gln Arg Asn Ala
65              70              75              80


Arg Gln Ser Lys Pro Phe Ala Ser Val Val Ala Gly Phe Ser Glu Leu
                85              90              95


Ala Trp Gln
```

```
<210>  2534
<211>  529
<212>  PRT
<213>  Homo sapiens
```

<400> 2534

Met Gly Ser Ser Arg Ala Pro Trp Met Gly Arg Val Gly Gly His Gly
1   5   10   15

Met Met Ala Leu Leu Leu Ala Gly Leu Leu Leu Pro Gly Thr Leu Ala
            20   25   30

Lys Ser Ile Gly Thr Phe Ser Asp Pro Cys Lys Asp Pro Thr Arg Ile
            35   40   45

Thr Ser Pro Asn Asp Pro Cys Leu Thr Gly Lys Gly Asp Ser Ser Gly
        50   55   60

Phe Ser Ser Tyr Ser Gly Ser Ser Ser Gly Ser Ser Ile Ser Ser
65   70   75   80

Ala Arg Ser Ser Gly Gly Gly Ser Ser Gly Ser Ser Ser Gly Ser Ser
                85   90   95

Ile Ala Gln Gly Gly Ser Ala Gly Ser Phe Lys Pro Gly Thr Gly Tyr
            100   105   110

Ser Gln Val Ser Tyr Ser Ser Gly Ser Gly Ser Ser Leu Gln Gly Ala
        115   120   125

Ser Gly Ser Ser Gln Leu Gly Ser Ser Ser Ser His Ser Gly Ser Ser
    130   135   140

Gly Ser His Ser Gly Ser Ser Ser Ser His Ser Ser Ser Ser Ser Ser
145   150   155   160

Phe Gln Phe Ser Ser Ser Ser Phe Gln Val Gly Asn Gly Ser Ala Leu
                165   170   175

Pro Thr Asn Asp Asn Ser Tyr Arg Gly Ile Leu Asn Pro Ser Gln Pro
            180   185   190

Gly Gln Ser Ser Ser Ser Ser Gln Thr Ser Gly Val Ser Ser Ser Gly
        195   200   205

Gln Ser Val Ser Ser Asn Gln Arg Pro Cys Ser Ser Asp Ile Pro Asp
    210   215   220

Ser Pro Cys Ser Gly Gly Pro Ile Val Ser His Ser Gly Pro Tyr Ile
225   230   235   240

```
Pro Ser Ser His Ser Val Ser Gly Gly Gln Arg Pro Val Val Val Val
            245             250             255

Val Asp Gln His Gly Ser Gly Ala Pro Gly Val Val Gln Gly Pro Pro
            260             265             270

Cys Ser Asn Gly Gly Leu Pro Gly Lys Pro Cys Pro Pro Ile Thr Ser
            275             280             285

Val Asp Lys Ser Tyr Gly Gly Tyr Glu Val Val Gly Gly Ser Ser Asp
    290             295             300

Ser Tyr Leu Val Pro Gly Met Thr Tyr Ser Lys Gly Lys Ile Tyr Pro
305             310             315             320

Val Gly Tyr Phe Thr Lys Glu Asn Pro Val Lys Gly Ser Pro Gly Val
            325             330             335

Pro Ser Phe Ala Ala Gly Pro Pro Ile Ser Glu Gly Lys Tyr Phe Ser
            340             345             350

Ser Asn Pro Ile Ile Pro Ser Gln Ser Ala Ala Ser Ser Ala Ile Ala
            355             360             365

Phe Gln Pro Val Gly Thr Gly Gly Val Gln Leu Cys Gly Gly Gly Ser
    370             375             380

Thr Gly Ser Lys Gly Pro Cys Ser Pro Ser Ser Ser Arg Val Pro Ser
385             390             395             400

Ser Ser Ser Ile Ser Ser Ser Ser Gly Ser Pro Tyr His Pro Cys Gly
            405             410             415

Ser Ala Ser Gln Ser Pro Cys Ser Pro Pro Gly Thr Gly Ser Phe Ser
            420             425             430

Ser Ser Ser Ser Ser Gln Ser Ser Gly Lys Ile Ile Leu Gln Pro Cys
            435             440             445

Gly Ser Lys Ser Ser Ser Ser Gly His Pro Cys Met Ser Val Ser Ser
    450             455             460

Leu Thr Leu Thr Gly Gly Pro Asp Gly Ser Pro His Pro Asp Pro Ser
465             470             475             480
```

903

```
Ala Gly Ala Lys Pro Cys Gly Ser Ser Ser Ala Gly Lys Ile Pro Cys
                485                 490                 495

Arg Ser Ile Arg Asp Ile Leu Ala Gln Val Lys Pro Leu Gly Pro Gln
            500                 505                 510

Leu Ala Asp Pro Glu Val Phe Leu Pro Gln Gly Glu Leu Leu Asp Ser
            515                 520                 525

Pro
```

```
<210>  2535
<211>  125
<212>  PRT
<213>  Homo sapiens

<400>  2535

Met Pro Pro Lys Asp Asp Lys Lys Lys Asp Ala Gly Lys Ser Ala
1               5                   10                  15

Lys Lys Asp Lys Asp Pro Val Asn Lys Ser Gly Gly Lys Ala Lys Lys
            20                  25                  30

Lys Lys Trp Ser Lys Gly Lys Val Arg Asp Lys Leu Asn Asn Leu Val
        35                  40                  45

Leu Phe Asp Lys Ala Thr Tyr Asp Lys Leu Cys Lys Glu Val Pro Asn
    50                  55                  60

Tyr Lys Leu Ile Thr Pro Ala Val Val Ser Glu Arg Leu Lys Ile Arg
65                  70                  75                  80

Gly Ser Leu Ala Arg Ala Ala Leu Gln Glu Leu Leu Ser Lys Gly Leu
                85                  90                  95

Ile Lys Leu Val Ser Lys His Arg Ala Gln Val Ile Tyr Thr Arg Asn
            100                 105                 110

Thr Lys Gly Gly Asp Ala Pro Ala Ala Gly Glu Asp Ala
        115                 120                 125
```

```
<210>  2536
<211>  335
<212>  PRT
<213>  Homo sapiens

<400>  2536
```

```
Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1               5                   10                  15

Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala
            20                  25                  30

Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
        35                  40                  45

Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Lys Ala Glu Asn
        50                  55                  60

Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65                  70                  75                  80

Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
            85                  90                  95

Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
            100                 105                 110

Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
        115                 120                 125

Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
    130                 135                 140

Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
145                 150                 155                 160

Ala Lys Val Ile His Asp Asn Phe Gly Ile Val Glu Gly Leu Met Thr
            165                 170                 175

Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
            180                 185                 190

Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
        195                 200                 205

Ala Ser Thr Gly Ala Ala Lys Ala Val Gly Lys Val Ile Pro Glu Leu
    210                 215                 220

Asn Gly Lys Leu Thr Gly Met Ala Phe Arg Val Pro Thr Ala Asn Val
225                 230                 235                 240
```

905

```
Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
              245               250               255

Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
          260           .   265               270

Ile Leu Gly Tyr Thr Glu His Gln Val Val Ser Ser Asp Phe Asn Ser
          275               280               285

Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
    290               295               300

Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
305               310               315               320

Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
              325               330               335
```

```
<210>    2537
<211>    114
<212>    PRT
<213>    Homo sapiens

<400>    2537
```

```
Met Ala Ser Val Ser Glu Leu Ala Cys Ile Tyr Ser Ala Leu Ile Leu
1                5                10               15

His Asp Asp Glu Val Thr Val Thr Glu Asp Lys Ile Asn Ala Leu Ile
              20               25               30

Lys Ala Ala Gly Val Asn Val Glu Pro Phe Trp Pro Gly Leu Phe Ala
          35               40               45

Lys Ala Leu Ala Asn Val Asn Ile Gly Ser Leu Ile Cys Asn Val Gly
          50               55               60

Ala Gly Gly Pro Ala Pro Ala Ala Gly Ala Ala Pro Ala Gly Gly Pro
65               70               75               80

Ala Pro Ser Thr Ala Ala Ala Pro Ala Glu Glu Lys Lys Val Glu Ala
              85               90               95

Lys Lys Glu Glu Ser Glu Glu Ser Asp Asp Asp Met Gly Phe Gly Leu
              100              105              110

Phe Asp
```

```
<210>   2538
<211>   142
<212>   PRT
<213>   Homo sapiens

<400>   2538

Met Ala Ala Gly Gly Ser Asp Pro Arg Ala Gly Asp Val Glu Glu Asp
1               5                   10                  15


Ala Ser Gln Leu Ile Phe Pro Lys Glu Phe Glu Thr Ala Glu Thr Leu
            20                  25                  30


Leu Asn Ser Glu Val His Met Leu Leu Glu His Arg Lys Gln Gln Asn
            35                  40                  45


Glu Ser Ala Glu Asp Glu Gln Glu Leu Ser Glu Val Phe Met Lys Thr
        50                  55                  60


Leu Asn Tyr Thr Ala Arg Phe Ser Arg Phe Lys Asn Arg Glu Thr Ile
65                  70                  75                  80


Ala Ser Val Arg Ser Leu Leu Leu Gln Lys Lys Leu His Lys Phe Glu
                85                  90                  95


Leu Ala Cys Leu Ala Asn Leu Cys Pro Glu Thr Ala Glu Glu Ser Lys
            100                 105                 110


Ala Leu Ile Pro Ser Leu Glu Gly Arg Phe Glu Asp Glu Glu Leu Gln
            115                 120                 125


Gln Ile Leu Asp Asp Ile Gln Thr Lys Arg Ser Phe Gln Tyr
        130                 135                 140


<210>   2539
<211>   178
<212>   PRT
<213>   Homo sapiens

<400>   2539

Met Pro Ala Tyr His Ser Ser Leu Met Asp Pro Asp Thr Lys Leu Ile
1               5                   10                  15


Gly Asn Met Ala Leu Leu Pro Ile Arg Ser Gln Phe Lys Gly Pro Ala
            20                  25                  30


Pro Arg Glu Thr Lys Asp Thr Asp Ile Val Asp Glu Ala Ile Tyr Tyr
```

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       35                        40                        45
```

Phe Lys Ala Asn Val Phe Phe Lys Asn Tyr Glu Ile Lys Asn Glu Ala
    50   55   60

Asp Arg Thr Leu Ile Tyr Ile Thr Leu Tyr Ile Ser Glu Cys Leu Lys
65   70   75   80

Lys Leu Gln Lys Cys Asn Ser Lys Ser Gln Gly Glu Lys Glu Met Tyr
                85   90   95

Thr Leu Gly Ile Thr Asn Phe Pro Ile Pro Gly Glu Pro Gly Phe Pro
                100   105   110

Leu Asn Ala Ile Tyr Ala Lys Pro Ala Asn Lys Gln Glu Asp Glu Val
            115   120   125

Met Arg Ala Tyr Leu Gln Gln Leu Arg Gln Glu Thr Gly Leu Arg Leu
        130   135   140

Cys Glu Lys Val Phe Asp Pro Gln Asn Asp Lys Pro Ser Lys Trp Trp
145   150   155   160

Thr Cys Phe Val Lys Arg Gln Phe Met Asn Lys Ser Leu Ser Gly Pro
                165   170   175

Gly Gln

<210> 2540
<211> 351
<212> PRT
<213> Homo sapiens

<400> 2540

Met Glu Thr Asn Phe Ser Thr Pro Leu Asn Glu Tyr Glu Glu Val Ser
1   5   10   15

Tyr Glu Ser Ala Gly Tyr Thr Val Leu Arg Ile Leu Pro Leu Val Val
                20   25   30

Leu Gly Val Thr Phe Val Leu Gly Val Leu Gly Asn Gly Leu Val Ile
                35   40   45

Trp Val Ala Gly Phe Arg Met Thr Arg Thr Val Thr Thr Ile Cys Tyr
        50   55   60

Leu Asn Leu Ala Leu Ala Asp Phe Ser Phe Thr Ala Thr Leu Pro Phe
65   70   75   80

Leu Ile Val Ser Met Ala Met Gly Glu Lys Trp Pro Phe Gly Trp Phe
                85   90   95

Leu Cys Lys Leu Ile His Ile Val Val Asp Ile Asn Leu Phe Gly Ser
            100   105   110

Val Phe Leu Ile Gly Phe Ile Ala Leu Asp Arg Cys Ile Cys Val Leu
        115   120   125

His Pro Val Trp Ala Gln Asn His Arg Thr Val Ser Leu Ala Met Lys
    130   135   140

Val Ile Val Gly Pro Trp Ile Leu Ala Leu Val Leu Thr Leu Pro Val
145   150   155   160

Phe Leu Phe Leu Thr Thr Val Thr Ile Pro Asn Gly Asp Thr Tyr Cys
            165   170   175

Thr Phe Asn Phe Ala Ser Trp Gly Gly Thr Pro Glu Glu Arg Leu Lys
            180   185   190

Val Ala Ile Thr Met Leu Thr Ala Arg Gly Ile Ile Arg Phe Val Ile
        195   200   205

Gly Phe Ser Leu Pro Met Ser Ile Val Ala Ile Cys Tyr Gly Leu Ile
    210   215   220

Ala Ala Lys Ile His Lys Lys Gly Met Ile Lys Ser Ser Arg Pro Leu
225   230   235   240

Arg Val Leu Thr Ala Val Val Ala Ser Phe Phe Ile Cys Trp Phe Pro
            245   250   255

Phe Gln Leu Val Ala Leu Leu Gly Thr Val Trp Leu Lys Glu Met Leu
            260   265   270

Phe Tyr Gly Lys Tyr Lys Ile Ile Asp Ile Leu Val Asn Pro Thr Ser
        275   280   285

Ser Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Met Leu Tyr Val Phe
    290   295   300

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```
Val Gly Gln Asp Phe Arg Glu Arg Leu Ile His Ser Leu Pro Thr Ser
305                 310                 315                 320


Leu Glu Arg Ala Leu Ser Glu Asp Ser Ala Pro Thr Asn Asp Thr Ala
                325                 330                 335


Ala Asn Ser Ala Ser Pro Pro Ala Glu Thr Glu Leu Gln Ala Met
                340                 345                 350
```

<210> 2541
<211> 349
<212> PRT
<213> Homo sapiens

<400> 2541

```
Met Glu Thr Pro Pro Val Asn Thr Ile Gly Glu Lys Asp Thr Ser Gln
1               5                   10                  15


Pro Gln Gln Glu Trp Glu Lys Asn Leu Arg Glu Asn Leu Asp Ser Val
                20                  25                  30


Ile Gln Ile Arg Gln Gln Pro Arg Asp Pro Pro Thr Glu Thr Leu Glu
            35                  40                  45


Leu Glu Val Ser Pro Asp Pro Ala Ser Gln Ile Leu Glu His Thr Gln
        50                  55                  60


Gly Ala Glu Lys Leu Val Ala Glu Leu Glu Gly Asp Ser His Lys Ser
65                  70                  75                  80


His Gly Ser Thr Ser Gln Met Pro Glu Ala Leu Gln Ala Ser Asp Leu
                85                  90                  95


Trp Tyr Cys Pro Asp Gly Ser Phe Val Lys Lys Ile Val Ile Arg Gly
            100                 105                 110


His Gly Leu Asp Lys Pro Lys Leu Gly Ser Cys Cys Arg Val Leu Ala
            115                 120                 125


Leu Gly Phe Pro Phe Gly Ser Gly Pro Pro Glu Gly Trp Thr Glu Leu
        130                 135                 140


Thr Met Gly Val Gly Pro Trp Arg Glu Glu Thr Trp Gly Glu Leu Ile
145                 150                 155                 160


Glu Lys Cys Leu Glu Ser Met Cys Gln Gly Glu Glu Ala Glu Leu Gln
                165                 170                 175
```

Leu Pro Gly His Ser Gly Pro Pro Val Arg Leu Thr Leu Ala Ser Phe
          180   185   190

Thr Gln Gly Arg Asp Ser Trp Glu Leu Glu Thr Ser Glu Lys Glu Ala
          195   200   205

Leu Ala Arg Glu Glu Arg Ala Arg Gly Thr Glu Leu Phe Arg Ala Gly
     210   215   220

Asn Pro Glu Gly Ala Ala Arg Cys Tyr Gly Arg Ala Leu Arg Leu Leu
225   230   235   240

Leu Thr Leu Pro Pro Pro Gly Pro Pro Glu Arg Thr Val Leu His Ala
               245   250   255

Asn Leu Ala Ala Cys Gln Leu Leu Leu Gly Gln Pro Gln Leu Ala Ala
          260   265   270

Gln Ser Cys Asp Arg Val Leu Glu Arg Glu Pro Gly His Leu Lys Ala
          275   280   285

Leu Tyr Arg Arg Gly Val Ala Gln Ala Ala Leu Gly Asn Leu Glu Lys
     290   295   300

Ala Thr Ala Asp Leu Lys Lys Val Leu Ala Ile Asp Pro Lys Asn Arg
305   310   315   320

Ala Ala Gln Glu Glu Leu Gly Lys Val Val Ile Gln Gly Lys Asn Gln
               325   330   335

Asp Ala Gly Leu Ala Gln Gly Leu Arg Lys Met Phe Gly
          340   345

<210> 2542
<211> 417
<212> PRT
<213> Homo sapiens

<400> 2542

Met Gly Arg Arg Arg Ala Pro Glu Leu Tyr Arg Ala Pro Phe Pro Leu
1   5   10   15

Tyr Ala Leu Gln Val Asp Pro Ser Thr Gly Leu Leu Ile Ala Ala Gly
          20   25   30

```
Gly Gly Gly Ala Ala Lys Thr Gly Ile Lys Asn Gly Val His Phe Leu
        35                  40                  45

Gln Leu Glu Leu Ile Asn Gly Arg Leu Ser Ala Ser Leu Leu His Ser
    50                  55                  60

His Asp Thr Glu Thr Arg Ala Thr Met Asn Leu Ala Leu Ala Gly Asp
65                  70                  75                  80

Ile Leu Ala Ala Gly Gln Asp Ala His Cys Gln Leu Leu Arg Phe Gln
            85                  90                  95

Ala His Gln Gln Gln Gly Asn Lys Ala Glu Lys Ala Gly Ser Lys Glu
            100                 105                 110

Gln Gly Pro Arg Gln Arg Lys Gly Ala Ala Pro Ala Glu Lys Lys Cys
        115                 120                 125

Gly Ala Glu Thr Gln His Glu Gly Leu Glu Leu Arg Val Glu Asn Leu
    130                 135                 140

Gln Ala Val Gln Thr Asp Phe Ser Ser Asp Pro Leu Gln Lys Val Val
145                 150                 155                 160

Cys Phe Asn His Asp Asn Thr Leu Leu Ala Thr Gly Gly Thr Asp Gly
            165                 170                 175

Tyr Val Arg Val Trp Lys Val Pro Ser Leu Glu Lys Val Leu Glu Phe
        180                 185                 190

Lys Ala His Glu Gly Glu Ile Glu Asp Leu Ala Leu Gly Pro Asp Gly
    195                 200                 205

Lys Leu Val Thr Val Gly Arg Asp Leu Lys Ala Ser Val Trp Gln Lys
210                 215                 220

Asp Gln Leu Val Thr Gln Leu His Trp Gln Glu Asn Gly Pro Thr Phe
225                 230                 235                 240

Ser Ser Thr Pro Tyr Arg Tyr Gln Ala Cys Arg Phe Gly Gln Val Pro
            245                 250                 255

Asp Gln Pro Ala Gly Leu Arg Leu Phe Thr Val Gln Ile Pro His Lys
        260                 265                 270

Arg Leu Arg Gln Pro Pro Pro Cys Tyr Leu Thr Ala Trp Asp Gly Ser
```

```
        275                    280                    285


Asn Phe Leu Pro Leu Arg Thr Lys Ser Cys Gly His Glu Val Val Ser
    290                    295                300


Cys Leu Asp Val Ser Glu Ser Gly Thr Phe Leu Gly Leu Gly Thr Val
305                    310                315                320


Thr Gly Ser Val Ala Ile Tyr Ile Ala Phe Ser Leu Gln Cys Leu Tyr
                325                330                335


Tyr Val Arg Glu Ala His Gly Ile Val Val Thr Asp Val Ala Phe Leu
            340                345                350


Pro Glu Lys Gly Arg Gly Pro Glu Leu Leu Gly Ser His Glu Thr Ala
        355                360                365


Leu Phe Ser Val Ala Val Asp Ser Arg Cys Gln Leu His Leu Leu Pro
    370                    375                380


Ser Arg Arg Ser Val Pro Val Trp Leu Leu Leu Leu Leu Cys Val Gly
385                    390                395                400


Leu Ile Ile Val Thr Ile Leu Leu Leu Gln Ser Ala Phe Pro Gly Phe
                405                410                415


Leu
```

```
<210>  2543
<211>  309
<212>  PRT
<213>  Homo sapiens

<400>  2543

Met Arg Gln Asn Asp Lys Ile Met Cys Ile Leu Glu Asn Arg Lys Lys
1                   5                   10                  15


Arg Asp Arg Lys Asn Leu Cys Arg Ala Ile Asn Asp Phe Gln Gln Ser
            20                  25                  30


Phe Gln Lys Pro Glu Thr Arg Arg Glu Phe Asp Leu Ser Asp Pro Leu
        35                  40                  45


Ala Leu Lys Lys Asp Leu Pro Ala Arg Gln Ser Asp Asn Asp Val Arg
    50                  55                  60
```

```
Asn Thr Ile Ser Gly Met Gln Lys Phe Met Gly Glu Asp Leu Asn Phe
65              70          75              80


His Glu Arg Lys Lys Phe Gln Glu Glu Gln Asn Arg Glu Trp Ser Leu
            85              90              95


Gln Gln Gln Arg Glu Trp Lys Asn Ala Arg Ala Glu Gln Lys Cys Ala
        100          .      105          110


Glu Ala Leu Tyr Thr Glu Thr Arg Leu Gln Phe Asp Glu Thr Ala Lys
        115              120          125


His Leu Gln Lys Leu Glu Ser Thr Thr Arg Lys Ala Val Cys Ala Ser
    130              135          140


Val Lys Asp Phe Asn Lys Ser Gln Ala Ile Glu Ser Val Glu Arg Lys
145              150          155              160


Lys Gln Glu Lys Lys Gln Glu Gln Glu Asp Asn Leu Ala Glu Ile Thr
            165              170          175


Asn Leu Leu Arg Gly Asp Leu Leu Ser Glu Asn Pro Gln Gln Ala Ala
        180              185          190


Ser Ser Phe Gly Pro His Arg Val Val Pro Asp Arg Trp Lys Gly Met
        195          200          205


Thr Gln Glu Gln Leu Glu Gln Ile Arg Leu Val Gln Lys Gln Gln Ile
    210              215          220


Gln Glu Lys Leu Arg Leu Gln Glu Glu Lys Arg Gln Arg Asp Leu Asp
225              230          235              240


Trp Asp Arg Arg Arg Ile Gln Gly Ala Arg Ala Thr Leu Leu Phe Glu
            245          250          255


Arg Gln Gln Trp Arg Arg Gln Arg Asp Leu Arg Arg Ala Leu Asp Ser
        260          265          270


Ser Asn Leu Ser Leu Ala Lys Glu Gln His Leu Gln Lys Lys Tyr Met
        275          280          285


Asn Glu Val Tyr Thr Asn Gln Pro Thr Gly Asp Tyr Phe Thr Gln Phe
    290              295          300
```

Asn Thr Gly Ser Arg
305

<210>   2544
<211>   838
<212>   PRT
<213>   Homo sapiens

<400>   2544

Met Gln Glu Gln Glu Ile Gly Phe Ile Ser Lys Tyr Asn Glu Gly Leu
1   5   10   15

Cys Val Asn Thr Asp Pro Val Ser Ile Leu Thr Ser Ile Leu Asp Met
            20   25   30

Ser Leu His Arg Gln Met Gly Ser Asp Arg Asp Leu Gln Ser Ser Ala
        35   40   45

Ser Ser Val Ser Leu Pro Ser Val Lys Lys Ala Pro Lys Lys Arg Arg
    50   55   60

Ile Ser Ile Gly Ser Leu Phe Arg Arg Lys Lys Asp Asn Lys Arg Lys
65   70   75   80

Ser Arg Glu Leu Asn Gly Gly Val Asp Gly Ile Ala Ser Ile Glu Ser
                85   90   95

Ile His Ser Glu Met Cys Thr Asp Lys Asn Ser Ile Phe Ser Thr Asn
            100   105   110

Thr Ser Ser Asp Asn Gly Leu Thr Ser Ile Ser Lys Gln Ile Gly Asp
        115   120   125

Phe Ile Glu Cys Pro Leu Cys Leu Leu Arg His Ser Lys Asp Arg Phe
    130   135   140

Pro Asp Ile Met Thr Cys His His Arg Ser Cys Val Asp Cys Leu Arg
145   150   155   160

Gln Tyr Leu Arg Ile Glu Ile Ser Glu Ser Arg Val Asn Ile Ser Cys
                165   170   175

Pro Glu Cys Thr Glu Arg Phe Asn Pro His Asp Ile Arg Leu Ile Leu
            180   185   190

Ser Asp Asp Val Leu Met Glu Lys Tyr Glu Glu Phe Met Leu Arg Arg
        195   200   205

Trp Leu Val Ala Asp Pro Asp Cys Arg Trp Cys Pro Ala Pro Asp Cys
    210   215   220

Gly Tyr Ala Val Ile Ala Phe Gly Cys Ala Ser Cys Pro Lys Leu Thr
225   230   235   240

Cys Gly Arg Glu Gly Cys Gly Thr Glu Phe Cys Tyr His Cys Lys Gln
            245   250   255

Ile Trp His Pro Asn Gln Thr Cys Asp Ala Ala Arg Gln Glu Arg Ala
            260   265   270

Gln Ser Leu Arg Leu Arg Thr Ile Arg Ser Ser Ser Ile Ser Tyr Ser
    275   280   285

Gln Glu Ser Gly Ala Ala Ala Asp Asp Ile Lys Pro Cys Pro Arg Cys
    290   295   300

Ala Ala Tyr Ile Ile Lys Met Asn Asp Gly Ser Cys Asn His Met Thr
305   310   315   320

Cys Ala Val Cys Gly Cys Glu Phe Cys Trp Leu Cys Met Lys Glu Ile
            325   330   335

Ser Asp Leu His Tyr Leu Ser Pro Ser Gly Cys Thr Phe Trp Gly Lys
            340   345   350

Lys Pro Trp Ser Arg Lys Lys Lys Ile Leu Trp Gln Leu Gly Thr Leu
            355   360   365

Val Gly Ala Pro Val Gly Ile Ala Leu Ile Ala Gly Ile Ala Ile Pro
    370   375   380

Ala Met Ile Ile Gly Ile Pro Val Tyr Val Gly Arg Lys Ile His Asn
385   390   395   400

Arg Tyr Glu Gly Lys Asp Val Ser Lys His Lys Arg Asn Leu Ala Ile
            405   410   415

Ala Gly Gly Val Thr Leu Ser Val Ile Val Ser Pro Val Val Ala Ala
            420   425   430

Val Thr Val Gly Ile Gly Val Pro Ile Met Leu Ala Tyr Val Tyr Gly
            435   440   445

```
Val Val Pro Ile Ser Leu Cys Arg Ser Gly Gly Cys Gly Val Ser Ala
    450             455             460

Gly Asn Gly Lys Gly Val Arg Ile Glu Phe Asp Asp Glu Asn Asp Ile
465             470             475             480

Asn Val Gly Gly Thr Asn Thr Ala Val Asp Thr Thr Ser Val Ala Glu
            485             490             495

Ala Arg His Asn Pro Ser Ile Gly Glu Gly Ser Val Gly Gly Leu Thr
        500             505             510

Gly Ser Leu Ser Ala Ser Gly Ser His Met Asp Arg Ile Gly Ala Ile
        515             520             525

Arg Asp Asn Leu Ser Glu Thr Ala Ser Thr Met Ala Leu Ala Gly Ala
    530             535             540

Ser Ile Thr Gly Ser Leu Ser Gly Ser Ala Met Val Asn Cys Phe Asn
545             550             555             560

Arg Leu Glu Val Gln Ala Asp Val Gln Lys Glu Arg Tyr Ser Leu Ser
            565             570             575

Gly Glu Ser Gly Thr Val Ser Leu Gly Thr Val Ser Asp Asn Ala Ser
            580             585             590

Thr Lys Ala Met Ala Gly Ser Ile Leu Asn Ser Tyr Ile Pro Leu Asp
        595             600             605

Lys Glu Gly Asn Ser Met Glu Val Gln Val Asp Ile Glu Ser Lys Pro
    610             615             620

Ser Lys Phe Arg His Asn Ser Gly Ser Ser Ser Val Asp Asp Gly Ser
625             630             635             640

Ala Thr Arg Ser Tyr Ala Gly Gly Ser Ser Ser Gly Leu Pro Glu Gly
            645             650             655

Lys Ser Ser Ala Thr Lys Trp Ser Lys Glu Ala Thr Ala Gly Lys Lys
        660             665             670

Ser Lys Ser Gly Lys Leu Arg Lys Lys Gly Asn Met Lys Ile Asn Glu
        675             680             685
```

```
Thr Arg Glu Asp Met Asp Ala Gln Leu Leu Glu Gln Gln Ser Thr Asn
    690             695             700

Ser Ser Glu Phe Glu Ala Pro Ser Leu Ser Asp Ser Met Pro Ser Val
705             710             715             720

Ala Asp Ser His Ser Ser His Phe Ser Glu Phe Ser Cys Ser Asp Leu
            725             730             735

Glu Ser Met Lys Thr Ser Cys Ser His Gly Ser Ser Asp Tyr His Thr
            740             745             750

Arg Phe Ala Thr Val Asn Ile Leu Pro Glu Val Glu Asn Asp Arg Leu
            755             760             765

Glu Asn Ser Pro His Gln Cys Ser Ile Ser Val Val Thr Gln Thr Ala
    770             775             780

Ser Cys Ser Glu Val Ser Gln Leu Asn His Ile Ala Glu Glu His Gly
785             790             795             800

Asn Asn Gly Ile Lys Pro Asn Val Asp Leu Tyr Phe Gly Asp Ala Leu
            805             810             815

Lys Glu Thr Asn Asn Asn His Ser His Gln Thr Met Glu Leu Lys Val
            820             825             830

Ala Ile Gln Thr Glu Ile
            835
```

```
<210>  2545
<211>  1539
<212>  PRT
<213>  Homo sapiens

<400>  2545
```

```
Met Glu Pro Gly Cys Asp Glu Phe Leu Pro Pro Glu Cys Pro Val
1           5           10          15

Phe Glu Pro Ser Trp Ala Glu Phe Gln Asp Pro Leu Gly Tyr Ile Ala
            20          25          30

Lys Ile Arg Pro Ile Ala Glu Lys Ser Gly Ile Cys Lys Ile Arg Pro
        35          40          45

Pro Ala Asp Trp Gln Pro Pro Phe Ala Val Glu Val Asp Asn Phe Arg
    50          55          60
```

Phe Thr Pro Arg Val Gln Arg Leu Asn Glu Leu Glu Ala Gln Thr Arg
65   70   75   80

Val Lys Leu Asn Tyr Leu Asp Gln Ile Ala Lys Phe Trp Glu Ile Gln
                85   90   95

Gly Ser Ser Leu Lys Ile Pro Asn Val Glu Arg Lys Ile Leu Asp Leu
            100   105   110

Tyr Ser Leu Ser Lys Ile Val Ile Glu Glu Gly Gly Tyr Glu Ala Ile
        115   120   125

Cys Lys Asp Arg Arg Trp Ala Arg Val Ala Gln Arg Leu His Tyr Pro
    130   135   140

Pro Gly Lys Asn Ile Gly Ser Leu Leu Arg Ser His Tyr Glu Arg Ile
145   150   155   160

Ile Tyr Pro Tyr Glu Met Phe Gln Ser Gly Ala Asn His Val Gln Cys
            165   170   175

Asn Thr His Pro Phe Asp Asn Glu Val Lys Asp Lys Glu Tyr Lys Pro
            180   185   190

His Ser Ile Pro Leu Arg Gln Ser Val Gln Pro Ser Lys Phe Ser Ser
        195   200   205

Tyr Ser Arg Arg Ala Lys Arg Leu Gln Pro Asp Pro Glu Pro Thr Glu
210   215   220

Glu Asp Ile Glu Lys His Pro Glu Leu Lys Lys Leu Gln Ile Tyr Gly
225   230   235   240

Pro Gly Pro Lys Met Met Gly Leu Gly Leu Met Ala Lys Asp Lys Asp
            245   250   255

Lys Thr Val His Lys Lys Val Thr Cys Pro Pro Thr Val Thr Val Lys
            260   265   270

Asp Glu Gln Ser Gly Gly Gly Asn Val Ser Ser Thr Leu Leu Lys Gln
        275   280   285

His Leu Ser Leu Glu Pro Cys Thr Lys Thr Thr Met Gln Leu Arg Lys
    290   295   300

Asn His Ser Ser Ala Gln Phe Ile Asp Ser Tyr Ile Cys Gln Val Cys
305   310   315   320

Ser Arg Gly Asp Glu Asp Asn Lys Leu Leu Phe Cys Asp Gly Cys Asp
                325   330   335

Asp Asn Tyr His Ile Phe Cys Leu Leu Pro Pro Leu Pro Glu Ile Pro
                340   . 345   350

Arg Gly Ile Trp Arg Cys Pro Lys Cys Ile Leu Ala Glu Cys Lys Gln
            355   360   365

Pro Pro Glu Ala Phe Gly Phe Glu Gln Ala Thr Gln Glu Tyr Ser Leu
    370   375   380

Gln Ser Phe Gly Glu Met Ala Asp Ser Phe Lys Ser Asp Tyr Phe Asn
385   390   395   400

Met Pro Val His Met Val Pro Thr Glu Leu Val Glu Lys Glu Phe Trp
                405   410   415

Arg Leu Val Ser Ser Ile Glu Glu Asp Val Thr Val Glu Tyr Gly Ala
            420   425   430

Asp Ile His Ser Lys Glu Phe Gly Ser Gly Phe Pro Val Ser Asn Ser
            435   440   445

Lys Gln Asn Leu Ser Pro Glu Glu Lys Glu Tyr Ala Thr Ser Gly Trp
    450   455   460

Asn Leu Asn Val Met Pro Val Leu Asp Gln Ser Val Leu Cys His Ile
465   470   475   480

Asn Ala Asp Ile Ser Gly Met Lys Val Pro Trp Leu Tyr Val Gly Met
            485   490   495

Val Phe Ser Ala Phe Cys Trp His Ile Glu Asp His Trp Ser Tyr Ser
            500   · 505   510

Ile Asn Tyr Leu His Trp Gly Glu Pro Lys Thr Trp Tyr Gly Val Pro
    515   520   525

Ser Leu Ala Ala Glu His Leu Glu Glu Val Met Lys Met Leu Thr Pro
    530   535   540

920

Glu Leu Phe Asp Ser Gln Pro Asp Leu Leu His Gln Leu Val Thr Leu
545   550   555   560

Met Asn Pro Asn Thr Leu Met Ser His Gly Val Pro Val Val Arg Thr
            565   570   575

Asn Gln Cys Ala Gly Glu Phe Val Ile Thr Phe Pro Arg Ala Tyr His
            580   585   590

Ser Gly Phe Asn Gln Gly Tyr Asn Phe Ala Glu Ala Val Asn Phe Cys
            595   600   605

Thr Ala Asp Trp Leu Pro Ala Gly Arg Gln Cys Ile Glu His Tyr Arg
    610   615   620

Arg Leu Arg Arg Tyr Cys Val Phe Ser His Glu Glu Leu Ile Cys Lys
625   630   635   640

Met Ala Ala Phe Pro Glu Thr Leu Asp Leu Asn Leu Ala Val Ala Val
            645   650   655

His Lys Glu Met Phe Ile Met Val Gln Glu Glu Arg Arg Leu Arg Lys
            660   665   670

Ala Leu Leu Glu Lys Gly Val Thr Glu Ala Glu Arg Glu Ala Phe Glu
            675   680   685

Leu Leu Pro Asp Asp Glu Arg Gln Cys Ile Lys Cys Lys Thr Thr Cys
    690   695   700

Phe Leu Ser Ala Leu Ala Cys Tyr Asp Cys Pro Asp Gly Leu Val Cys
705   710   715   720

Leu Ser His Ile Asn Asp Leu Cys Lys Cys Ser Ser Ser Arg Gln Tyr
            725   730   735

Leu Arg Tyr Arg Tyr Thr Leu Asp Glu Leu Pro Thr Met Leu His Lys
            740   745   750

Leu Lys Ile Arg Ala Glu Ser Phe Asp Thr Trp Ala Asn Lys Val Arg
            755   760   765

Val Ala Leu Glu Val Glu Asp Gly Arg Lys Arg Ser Phe Glu Glu Leu
    770   775   780

Arg Ala Leu Glu Ser Glu Ala Arg Glu Arg Arg Phe Pro Asn Ser Glu

785   790   795   800

Leu Leu Gln Arg Leu Lys Asn Cys Leu Ser Glu Val Glu Ala Cys Ile
            805   810   815

Ala Gln Val Leu Gly Leu Val Ser Gly Gln Val Ala Arg Met Asp Thr
            820   825   830

Pro Gln Leu Thr Leu Thr Glu Leu Arg Val Leu Leu Glu Gln Met Gly
            835   840   845

Ser Leu Pro Cys Ala Met His Gln Ile Gly Asp Val Lys Asp Val Leu
            850   855   860

Glu Gln Val Glu Ala Tyr Gln Ala Glu Ala Arg Glu Ala Leu Ala Thr
865   870   875   880

Leu Pro Ser Ser Pro Gly Leu Leu Arg Ser Leu Leu Glu Arg Gly Gln
            885   890   895

Gln Leu Gly Val Glu Val Pro Glu Ala His Gln Leu Gln Gln Gln Val
            900   905   910

Glu Gln Ala Gln Trp Leu Asp Glu Val Lys Gln Ala Leu Ala Pro Ser
            915   920   925

Ala His Arg Gly Ser Leu Val Ile Met Gln Gly Leu Leu Val Met Gly
            930   935   940

Ala Lys Ile Ala Ser Ser Pro Ser Val Asp Lys Ala Arg Ala Glu Leu
945   950   955   960

Gln Glu Leu Leu Thr Ile Ala Glu Arg Trp Glu Glu Lys Ala His Phe
            965   970   975

Cys Leu Glu Ala Arg Gln Lys His Pro Pro Ala Thr Leu Glu Ala Ile
            980   985   990

Ile Arg Glu Thr Glu Asn Ile Pro Val His Leu Pro Asn Ile Gln Ala
            995   1000   1005

Leu Lys Glu Ala Leu Thr Lys Ala Gln Ala Trp Ile Ala Asp Val
    1010   1015   1020

Asp Glu Ile Gln Asn Gly Asp His Tyr Pro Cys Leu Asp Asp Leu
    1025   1030   1035

922

```
Glu Gly Leu Val Ala Val Gly Arg Asp Leu Pro Val Gly Leu Glu
    1040             1045             1050


Glu Leu Arg Gln Leu Glu Leu Gln Val Leu Thr Ala His Ser Trp
    1055             1060             1065


Arg Glu Lys Ala Ser Lys Thr Phe Leu Lys Lys Asn Ser Cys Tyr
    1070             1075             1080


Thr Leu Leu Glu Val Leu Cys Pro Cys Ala Asp Ala Gly Ser Asp
    1085             1090             1095


Ser Thr Lys Arg Ser Arg Trp Met Glu Lys Ala Leu Gly Leu Tyr
    1100             1105             1110


Gln Cys Asp Thr Glu Leu Leu Gly Leu Ser Ala Gln Asp Leu Arg
    1115             1120             1125


Asp Pro Gly Ser Val Ile Val Ala Phe Lys Glu Gly Glu Gln Lys
    1130             1135             1140


Glu Lys Glu Gly Ile Leu Gln Leu Arg Arg Thr Asn Ser Ala Lys
    1145             1150             1155


Pro Ser Pro Leu Ala Pro Ser Leu Met Ala Ser Ser Pro Thr Ser
    1160             1165             1170


Ile Cys Val Cys Gly Gln Val Pro Ala Gly Val Gly Leu Leu Gln
    1175             1180             1185


Cys Asp Leu Cys Gln Asp Trp Phe His Gly Gln Cys Val Ser Val
    1190             1195             1200


Pro His Leu Leu Thr Ser Pro Lys Pro Ser Leu Thr Ser Ser Pro
    1205             1210             1215


Leu Leu Ala Trp Trp Glu Trp Asp Thr Lys Phe Leu Cys Pro Leu
    1220             1225             1230


Cys Met Arg Ser Arg Arg Pro Arg Leu Glu Thr Ile Leu Ala Leu
    1235             1240             1245


Leu Val Ala Leu Gln Arg Leu Pro Val Arg Leu Pro Glu Gly Glu
    1250             1255             1260
```

                                        923

```
Ala Leu  Gln Cys Leu Thr Glu  Arg Ala Ile Gly Trp  Gln Asp Arg
    1265              1270              1275


Ala Arg  Lys Ala Leu Ala Phe  Glu Asp Val Thr Ala  Leu Leu Arg
    1280              1285              1290


Gln Leu  Ala Glu Leu Arg Gln  Gln Leu Gln Ala Lys  Pro Arg Pro
    1295              1300              1305


Glu Glu  Ala Ser Val Tyr Thr  Ser Ala Thr Ala Cys  Asp Pro Ile
    1310              1315              1320


Arg Glu  Gly Ser Gly Asn Asn  Ile Ser Lys Val Gln  Gly Leu Leu
    1325              1330              1335


Glu Asn  Gly Asp Ser Val Thr  Ser Pro Glu Asn Met  Ala Pro Gly
    1340              1345              1350


Lys Gly  Ser Asp Leu Glu Leu  Leu Ser Ser Leu Leu  Pro Gln Leu
    1355              1360              1365


Thr Gly  Pro Val Leu Glu Leu  Pro Glu Ala Ile Arg  Ala Pro Leu
    1370              1375              1380


Glu Glu  Leu Met Met Glu Gly  Gly Leu Leu Glu Val  Thr Leu Asp
    1385              1390              1395


Glu Asn  His Ser Ile Trp Gln  Leu Leu Gln Ala Gly  Gln Pro Pro
    1400              1405              1410


Asp Leu  Asp Arg Ile Arg Thr  Leu Leu Glu Leu Glu  Lys Phe Glu
    1415              1420              1425


His Gln  Gly Ser Arg Thr Arg  Ser Arg Ala Leu Glu  Arg Arg Arg
    1430              1435              1440


Arg Arg  Gln Lys Val Asp Gln  Gly Arg Asn Val Glu  Asn Leu Val
    1445              1450              1455


Gln Gln  Glu Leu Gln Ser Lys  Arg Ala Arg Ser Ser  Gly Ile Met
    1460              1465              1470


Ser Gln  Val Gly Arg Glu Glu  Glu His Tyr Gln Glu  Lys Ala Asp
    1475              1480              1485
```

```
Arg Glu  Asn Met Phe Leu Thr  Pro Ser Thr Asp His  Ser Pro Phe
    1490                 1495             1500


Leu Lys  Gly Asn Gln Asn Ser  Leu Gln His Lys Asp  Ser Gly Ser
    1505                 1510             1515


Ser Ala  Ala Cys Pro Ser Leu  Met Pro Leu Leu Gln  Leu Ser Tyr
    1520                 1525             1530


Ser Asp  Glu Gln Gln Leu
    1535



<210>  2546
<211>  274
<212>  PRT
<213>  Homo sapiens


<400>  2546

Met Gly Val Ser Ala Gln Asp Ile Phe Asn Ala Val Ile Lys Glu His
1             5             10             15


Pro Gly Leu Val Gln Arg Leu Pro Cys Val Trp Asn Val Gln Leu Ser
        20             25             30


Asp His Thr Leu Ala Glu Arg Cys Tyr Ser Glu Ala Ser Asp Leu Lys
        35             40             45


Val Ile His Trp Asn Ser Pro Lys Lys Leu Arg Val Lys Asn Lys His
    50             55             60


Val Glu Phe Phe Arg Asn Phe Tyr Leu Thr Phe Leu Glu Tyr Asp Gly
65             70             75             80


Asn Leu Leu Arg Arg Glu Leu Phe Val Cys Pro Ser Gln Pro Pro Pro
            85             90             95


Gly Ala Glu Gln Leu Gln Gln Ala Leu Ala Gln Leu Asp Gly Glu Asp
            100            105            110


Pro Cys Phe Glu Phe Arg Gln Gln Gln Leu Thr Val His Arg Val His
        115            120            125


Val Thr Phe Leu Pro His Glu Pro Pro Pro Arg Pro His Asp Val
    130            135            140


Thr Leu Val Ala Gln Leu Ser Met Asp Arg Leu Gln Met Leu Glu Ala
145            150            155            160
```

Leu Cys Arg His Trp Pro Gly Pro Met Ser Leu Ala Leu Tyr Leu Thr
                165   170   175

Asp Ala Glu Ala Gln Gln Phe Leu His Phe Val Glu Ala Ser Pro Val
            180   185   190

Leu Ala Ala Arg Gln Asp Val Ala Tyr His Val Val Tyr Arg Glu Gly
        195   200   205

Pro Leu Tyr Pro Val Asn Gln Leu Arg Asn Val Ala Leu Ala Gln Ala
    210   215   220

Leu Thr Pro Tyr Val Phe Leu Ser Asp Ile Asp Phe Leu Pro Ala Tyr
225   230   235   240

Ser Leu Tyr Asp Tyr Leu Arg Glu Ala Arg Ala Gly Phe Asn Ser Ser
            245   250   255

Ser Thr Cys Gly Cys Ala His Pro Ser His Gln Ala Arg Trp Pro Met
            260   265   270

Val Val

<210> 2547
<211> 504
<212> PRT
<213> Homo sapiens

<400> 2547

Met Val Ala Pro Gly Ser Val Thr Ser Arg Leu Gly Ser Val Phe Pro
1   5   10   15

Phe Leu Leu Val Leu Val Asp Leu Gln Tyr Glu Gly Ala Glu Cys Gly
            20   25   30

Val Asn Ala Asp Val Glu Lys His Leu Glu Leu Gly Lys Lys Leu Leu
        35   40   45

Ala Ala Gly Gln Leu Ala Asp Ala Leu Ser Gln Phe His Ala Ala Val
    50   55   60

Asp Gly Asp Pro Asp Asn Tyr Ile Ala Tyr Tyr Arg Arg Ala Thr Val
65   70   75   80

Phe Leu Ala Met Gly Lys Ser Lys Ala Ala Leu Pro Asp Leu Thr Lys
                85   90   95

Val Ile Gln Leu Lys Met Asp Phe Thr Ala Ala Arg Leu Gln Arg Gly
            100   105   110

His Leu Leu Leu Lys Gln Gly Lys Leu Asp Glu Ala Glu Asp Asp Phe
        115   120   125

Lys Lys Val Leu Lys Ser Asn Pro Ser Glu Asn Glu Glu Lys Glu Ala
    130   135   140

Gln Ser Gln Leu Ile Lys Ser Asp Glu Met Gln Arg Leu Arg Ser Gln
145   150   155   160

Ala Leu Asn Ala Phe Gly Ser Gly Asp Tyr Thr Ala Ala Ile Ala Phe
            165   170   175

Leu Asp Lys Ile Leu Glu Val Cys Val Trp Asp Ala Glu Leu Arg Glu
            180   185   190

Leu Arg Ala Glu Cys Phe Ile Lys Glu Gly Glu Pro Arg Lys Ala Ile
        195   200   205

Ser Asp Leu Lys Ala Ala Ser Lys Leu Lys Asn Asp Asn Thr Glu Ala
    210   215   220

Phe Tyr Lys Ile Ser Thr Leu Tyr Tyr Gln Leu Gly Asp His Glu Leu
225   230   235   240

Ser Leu Ser Glu Val Arg Glu Cys Leu Lys Leu Asp Gln Asp His Lys
            245   250   255

Arg Cys Phe Ala His Tyr Lys Gln Val Lys Lys Leu Asn Lys Leu Ile
            260   265   270

Glu Ser Ala Glu Glu Leu Ile Arg Asp Gly Arg Tyr Thr Asp Ala Thr
    275   280   285

Ser Lys Tyr Glu Ser Val Met Lys Thr Glu Pro Ser Ile Ala Glu Tyr
    290   295   300

Thr Val Arg Ser Lys Glu Arg Ile Cys His Cys Phe Ser Lys Asp Glu
 305   310   315   320

Lys Pro Val Glu Ala Ile Arg Val Cys Ser Glu Val Leu Gln Met Glu

927

```
                    325                 330                 335


    Pro Asp Asn Val Asn Ala Leu Lys Asp Arg Ala Glu Ala Tyr Leu Ile
            340                 345                 350


    Glu Glu Met Tyr Asp Glu Ala Ile Gln Asp Tyr Glu Thr Ala Gln Glu
            355                 360                 365


    His Asn Glu Asn Asp Gln Gln Ile Arg Glu Gly Leu Glu Lys Ala Gln
        370                 375                 380


    Arg Leu Leu Lys Gln Ser Gln Lys Arg Asp Tyr Tyr Lys Ile Leu Gly
    385                 390                 395                 400


    Val Lys Arg Asn Ala Lys Lys Gln Glu Ile Ile Lys Ala Tyr Arg Lys
                405                 410                 415


    Leu Ala Leu Gln Trp His Pro Asp Asn Phe Gln Asn Glu Glu Glu Lys
                420                 425                 430


    Lys Lys Ala Glu Lys Lys Phe Ile Asp Ile Ala Ala Ala Lys Glu Val
                435                 440                 445


    Leu Ser Asp Pro Glu Met Arg Lys Lys Phe Asp Asp Gly Glu Asp Pro
        450                 455                 460


    Leu Asp Ala Glu Ser Gln Gln Gly Gly Gly Gly Asn Pro Phe His Arg
    465                 470                 475                 480


    Ser Trp Asn Ser Trp Gln Gly Phe Asn Pro Phe Ser Ser Gly Gly Pro
                485                 490                 495


    Phe Arg Phe Lys Phe His Phe Asn
                500


    <210>  2548
    <211>  258
    <212>  PRT
    <213>  Homo sapiens

    <400>  2548

    Met Pro Pro Gln Gln Gly Asp Pro Ala Phe Pro Asp Arg Cys Glu Ala
    1               5                   10                  15


    Pro Pro Val Pro Pro Arg Arg Glu Arg Gly Gly Arg Gly Gly Arg Gly
                20                  25                  30
```

```
Pro Gly Glu Pro Gly Gly Arg Gly Arg Ala Gly Gly Ala Glu Gly Arg
        35              40              45
```

```
Gly Val Lys Cys Val Leu Val Gly Asp Gly Ala Val Gly Lys Thr Ser
    50              55              60
```

```
Leu Val Val Ser Tyr Thr Thr Asn Gly Tyr Pro Thr Glu Tyr Ile Pro
65              70              75                      80
```

```
Thr Ala Phe Asp Asn Phe Ser Ala Val Val Ser Val Asp Gly Arg Pro
            85              90              95
```

```
Val Arg Leu Gln Leu Cys Asp Thr Ala Gly Gln Asp Glu Phe Asp Lys
        100             105             110
```

```
Leu Arg Pro Leu Cys Tyr Thr Asn Thr Asp Ile Phe Leu Leu Cys Phe
        115             120             125
```

```
Ser Val Val Ser Pro Ser Ser Phe Gln Asn Val Ser Glu Lys Trp Val
    130             135             140
```

```
Pro Glu Ile Arg Cys His Cys Pro Lys Ala Pro Ile Ile Leu Val Gly
145             150             155             160
```

```
Thr Gln Ser Asp Leu Arg Glu Asp Val Lys Val Leu Ile Glu Leu Asp
            165             170             175
```

```
Lys Cys Lys Glu Lys Pro Val Pro Glu Glu Ala Ala Lys Leu Cys Ala
        180             185             190
```

```
Glu Glu Ile Lys Ala Ala Ser Tyr Ile Glu Cys Ser Ala Leu Thr Gln
        195             200             205
```

```
Lys Asn Leu Lys Glu Val Phe Asp Ala Ala Ile Val Ala Gly Ile Gln
    210             215             220
```

```
Tyr Ser Asp Thr Gln Gln Gln Pro Lys Lys Ser Lys Ser Arg Thr Pro
225             230             235             240
```

```
Asp Lys Met Lys Asn Leu Ser Lys Ser Trp Trp Lys Lys Tyr Cys Cys
            245             250             255
```

```
Phe Val
```

929

<210> 2549
<211> 394
<212> PRT
<213> Homo sapiens

<400> 2549

Met Phe Lys Lys Lys Ser His Val Arg Asn His Leu Arg Thr His Thr
1   5   10   15

Gly Glu Arg Pro Phe Pro Cys Pro Asp Cys Ser Lys Pro Phe Asn Ser
                20   25   30

Pro Ala Asn Leu Ala Arg His Arg Leu Thr His Thr Gly Glu Arg Pro
            35   40   45

Tyr Arg Cys Gly Asp Cys Gly Lys Ala Phe Thr Gln Ser Ser Thr Leu
    50   55   60

Arg Gln His Arg Leu Val His Ala Gln His Phe Pro Tyr Arg Cys Gln
65   70   75   80

Glu Cys Gly Val Arg Phe His Arg Pro Tyr Arg Leu Leu Met His Arg
                85   90   95

Tyr His His Thr Gly Glu Tyr Pro Tyr Lys Cys Arg Glu Cys Pro Arg
                100   105   110

Ser Phe Leu Leu Arg Arg Leu Leu Glu Val His Gln Leu Val Val His
            115   120   125

Ala Gly Arg Gln Pro His Arg Cys Pro Ser Cys Gly Ala Ala Phe Pro
    130   135   140

Ser Ser Leu Arg Leu Arg Glu His Arg Cys Ala Ala Ala Ala Ala Gln
145   150   155   160

Ala Pro Arg Arg Phe Glu Cys Gly Thr Cys Gly Lys Lys Val Gly Ser
                165   170   175

Ala Ala Arg Leu Gln Ala His Glu Ala Ala His Ala Ala Ala Gly Pro
            180   185   190

Gly Glu Val Leu Ala Lys Glu Pro Pro Ala Pro Arg Ala Pro Arg Ala
            195   200   205

Thr Arg Ala Pro Val Ala Ser Pro Ala Ala Leu Gly Ser Thr Ala Thr
    210   215   220

930

Ala Ser Pro Ala Ala Pro Ala Arg Arg Arg Gly Leu Glu Cys Ser Glu
225   230   235   240

Cys Lys Lys Leu Phe Ser Thr Glu Thr Ser Leu Gln Val His Arg Arg
            245   250   255

Ile His Thr Gly Glu Arg Pro Tyr Pro Cys Pro Asp Cys Gly Lys Ala
            260   265   270

Phe Arg Gln Ser Thr His Leu Lys Asp His Arg Arg Leu His Thr Gly
        275   280   285

Glu Arg Pro Phe Ala Cys Glu Val Cys Gly Lys Ala Phe Ala Ile Ser
    290   295   300

Met Arg Leu Ala Glu His Arg Arg Ile His Thr Gly Glu Arg Pro Tyr
305   310   315   320

Ser Cys Pro Asp Cys Gly Lys Ser Tyr Arg Ser Phe Ser Asn Leu Trp
            325   330   335

Lys His Arg Lys Thr His Gln Gln Gln His Gln Ala Ala Val Arg Gln
            340   345   350

Gln Leu Ala Glu Ala Glu Ala Ala Val Gly Leu Ala Val Met Glu Thr
        355   360   365

Ala Val Glu Ala Leu Pro Leu Val Glu Ala Ile Glu Ile Tyr Pro Leu
    370   375   380

Ala Glu Ala Glu Gly Val Gln Ile Ser Gly
385   390

<210>   2550
<211>   415
<212>   PRT
<213>   Homo sapiens

<400>   2550

Met Glu Asp Leu Cys Val Ala Asn Thr Leu Phe Ala Leu Asn Leu Phe
1   5   10   15

Lys His Leu Ala Lys Ala Ser Pro Thr Gln Asn Leu Phe Leu Ser Pro
            20   25   30

Trp Ser Ile Ser Ser Thr Met Ala Met Val Tyr Met Gly Ser Arg Gly
        35   40   45

Ser Thr Glu Asp Gln Met Ala Lys Val Leu Gln Phe Asn Glu Val Gly
    50   55   60

Ala Asn Ala Val Thr Pro Met Thr Pro Glu Asn Phe Thr Ser Cys Gly
65   70   75   80

Phe Met Gln Gln Ile Gln Lys Gly Ser Tyr Pro Asp Ala Ile Leu Gln
                85   90   95

Ala Gln Ala Ala Asp Lys Ile His Ser Ser Phe Arg Ser Leu Ser Ser
            100   105   110

Ala Ile Asn Ala Ser Thr Gly Asn Tyr Leu Leu Glu Ser Val Asn Lys
        115   120   125

Leu Phe Gly Glu Lys Ser Ala Ser Phe Arg Glu Glu Tyr Ile Arg Leu
    130   135   140

Cys Gln Lys Tyr Tyr Ser Ser Glu Pro Gln Ala Val Asp Phe Leu Glu
145   150   155   160

Cys Ala Glu Glu Ala Arg Lys Lys Ile Asn Ser Trp Val Lys Thr Gln
            165   170   175

Thr Lys Gly Lys Ile Pro Asn Leu Leu Pro Glu Gly Ser Val Asp Gly
            180   185   190

Asp Thr Arg Met Val Leu Val Asn Ala Val Tyr Phe Lys Gly Lys Trp
        195   200   205

Lys Thr Pro Phe Glu Lys Lys Leu Asn Gly Leu Tyr Pro Phe Arg Val
    210   215   220

Asn Ser Ala Gln Arg Thr Pro Val Gln Met Met Tyr Leu Arg Glu Lys
225   230   235   240

Leu Asn Ile Gly Tyr Ile Glu Asp Leu Lys Ala Gln Ile Leu Glu Leu
            245   250   255

Pro Tyr Ala Gly Asp Val Ser Met Phe Leu Leu Leu Pro Asp Glu Ile
        260   265   270

Ala Asp Val Ser Thr Gly Leu Glu Leu Leu Glu Ser Glu Ile Thr Tyr

```
        275                 280                 285


Asp Lys Leu Asn Lys Trp Thr Ser Lys Asp Lys Met Ala Glu Asp Glu
    290                 295                 300


Val Glu Val Tyr Ile Pro Gln Phe Lys Leu Glu Glu His Tyr Glu Leu
305                 310                 315                 320


Arg Ser Ile Leu Arg Ser Met Gly Met Glu Asp Ala Phe Asn Lys Gly
                325                 330                 335


Arg Ala Asn Phe Ser Gly Met Ser Glu Arg Asn Asp Leu Phe Leu Ser
                340                 345                 350


Glu Val Phe His Gln Ala Met Val Asp Val Asn Glu Glu Gly Thr Glu
            355                 360                 365


Ala Ala Ala Gly Thr Gly Gly Val Met Thr Gly Arg Thr Gly His Gly
        370                 375                 380


Gly Pro Gln Phe Val Ala Asp His Pro Phe Leu Phe Leu Ile Met His
385                 390                 395                 400


Lys Ile Thr Asn Cys Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
                405                 410                 415


<210>  2551
<211>  434
<212>  PRT
<213>  Homo sapiens

<400>  2551

Met Ser Ile Leu Lys Ile His Ala Arg Glu Ile Phe Asp Ser Arg Gly
1               5                   10                  15


Asn Pro Thr Val Glu Val Asp Leu Phe Thr Ser Lys Gly Leu Phe Arg
                20                  25                  30


Ala Ala Val Pro Ser Gly Ala Ser Thr Gly Ile Tyr Glu Ala Leu Glu
            35                  40                  45


Leu Arg Asp Asn Asp Lys Thr Arg Tyr Met Gly Lys Gly Val Ser Lys
        50                  55                  60


Ala Val Glu His Ile Asn Lys Thr Ile Ala Pro Ala Leu Val Ser Lys
65                  70                  75                  80
```

Lys Leu Asn Val Thr Glu Gln Glu Lys Ile Asp Lys Leu Met Ile Glu
                    85   90   95

Met Asp Gly Thr Glu Asn Lys Ser Lys Phe Gly Ala Asn Ala Ile Leu
                100   105   110

Gly Val Ser Leu Ala Val Cys Lys Ala Gly Ala Val Glu Lys Gly Val
            115   120   125

Pro Leu Tyr Arg His Ile Ala Asp Leu Ala Gly Asn Ser Glu Val Ile
    130   135   140

Leu Pro Val Pro Ala Phe Asn Val Ile Asn Gly Gly Ser His Ala Gly
145   150   155   160

Asn Lys Leu Ala Met Gln Glu Phe Met Ile Leu Pro Val Gly Ala Ala
                165   170   175

Asn Phe Arg Glu Ala Met Arg Ile Gly Ala Glu Val Tyr His Asn Leu
                180   185   190

Lys Asn Val Ile Lys Glu Lys Tyr Gly Lys Asp Ala Thr Asn Val Gly
            195   200   205

Asp Glu Gly Gly Phe Ala Pro Asn Ile Leu Glu Asn Lys Glu Gly Leu
    210   215   220

Glu Leu Leu Lys Thr Ala Ile Gly Lys Ala Gly Tyr Thr Asp Lys Val
225   230   235   240

Val Ile Gly Met Asp Val Ala Ala Ser Glu Phe Phe Arg Ser Gly Lys
                245   250   255

Tyr Asp Leu Asp Phe Lys Ser Pro Asp Asp Pro Ser Arg Tyr Ile Ser
            260   265   270

Pro Asp Gln Leu Ala Asp Leu Tyr Lys Ser Phe Ile Lys Asp Tyr Pro
            275   280   285

Val Val Ser Ile Glu Asp Pro Phe Asp Gln Asp Asp Trp Gly Ala Trp
    290   295   300

Gln Lys Phe Thr Ala Ser Ala Gly Ile Gln Val Val Gly Asp Asp Leu
305   310   315   320

```
Thr Val Thr Asn Pro Lys Arg Ile Ala Lys Ala Val Asn Glu Lys Ser
              325             330             335


Cys Asn Cys Leu Leu Leu Lys Val Asn Gln Ile Gly Ser Val Thr Glu
              340             345             350


Ser Leu Gln Ala Cys Lys Leu Ala Gln Ala Asn Gly Trp Gly Val Met
          355             360             365


Val Ser His Arg Ser Gly Glu Thr Glu Asp Thr Phe Ile Ala Asp Leu
      370             375             380


Val Val Gly Leu Cys Thr Gly Gln Ile Lys Thr Gly Ala Pro Cys Arg
385             390             395             400


Ser Glu Arg Leu Ala Lys Tyr Asn Gln Leu Leu Arg Ile Glu Glu Glu
              405             410             415


Leu Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn Pro Leu
              420             425             430


Ala Lys
```

```
<210> 2552
<211> 281
<212> PRT
<213> Homo sapiens

<400> 2552
```

```
Met Glu Val His Gln Gln Asn Ala Leu Phe Gln Tyr Phe Ala Asp Thr
1               5               10              15


Leu Thr Ala Val Val Gln Asn Ala Lys Lys Asn Gly Arg Tyr Asp Met
              20              25              30


Gly Ile Leu Asp Leu Gly Ser Gly Asp Glu Lys Val Arg Lys Ser Asp
          35              40              45


Val Lys Lys Phe Leu Thr Pro Gly Tyr Ser Thr Ser Gly His Val Glu
      50              55              60


Leu Tyr Thr Ile Ser Val Glu Arg Gly Met Ser Trp Glu Glu Ala Thr
65              70              75              80


Lys Ile Trp Ala Glu Leu Thr Gly Pro Asp Asp Gly Phe Tyr Leu Ser
              85              90              95
```

```
Leu Gln Ile Arg Asn Asn Lys Lys Thr Ala Ile Leu Val Lys Glu Val
            100             .           105             110


Asn Pro Lys Lys Lys Leu Phe Leu Val Tyr Arg Pro Asn Thr Gly Lys
            115             120             125                    `


Gln Leu Lys Leu Glu Ile Tyr Ala Asp Leu Lys Lys Lys Tyr Lys Lys
            130             135             140


Val Val Ser Asp Asp Ala Leu Met His Trp Leu Asp Gln Tyr Asn Ser
145             150             155                 160


Ser Ala Asp Thr Cys Thr His Ala Tyr Trp Arg Gly Asn Cys Lys Lys
                165             170             175


Ala Ser Leu Gly Leu Val Cys Glu Ile Gly Leu Arg Cys Arg Thr Tyr
            180             185             190


Tyr Val Leu Cys Gly Ser Val Leu Ser Val Trp Thr Lys Val Glu Gly
            195             200             205


Val Leu Ala Ser Val Ser Gly Thr Asn Val Lys Met Gln Ile Val Arg
            210             215             220


Leu Arg Thr Glu Asp Gly Gln Arg Ile Val Gly Leu Ile Ile Pro Ala
225                 230             235                 240


Asn Cys Val Ser Pro Leu Val Asn Leu Leu Ser Thr Ser Asp Gln Ser
                245             250             255


Gln Gln Leu Ala Val Gln Gln Lys Gln Leu Trp Gln Gln His His Pro
            260             265             270


Gln Ser Ile Thr Asn Leu Ser Asn Ala
            275             280


<210> 2553
<211> 176
<212> PRT
<213> Homo sapiens


<400> 2553


Met Lys Ala Ser Gly Thr Leu Arg Glu Tyr Lys Val Val Gly Arg Cys
1               5               10              15
```

Leu Pro Thr Pro Lys Cys His Thr Pro Pro Leu Tyr Arg Met Arg Ile
             20   25   30

Phe Ala Pro Asn His Val Val Ala Lys Ser Arg Phe Trp Tyr Phe Val
         35   40   45

Ser Gln Leu Lys Lys Met Lys Lys Ser Ser Gly Glu Ile Val Tyr Cys
     50   55   60

Gly Gln Val Phe Glu Lys Ser Pro Leu Arg Val Lys Asn Phe Gly Ile
65   70   75   80

Trp Leu Arg Tyr Asp Ser Arg Ser Gly Thr His Asn Met Tyr Arg Glu
             85   90   95

Tyr Arg Asp Leu Thr Thr Ala Gly Ala Val Thr Gln Cys Tyr Arg Asp
         100   105   110

Met Gly Ala Arg His Arg Ala Arg Ala His Ser Ile Gln Ile Met Lys
         115   120   125

Val Glu Glu Ile Ala Ala Ser Lys Cys Arg Arg Pro Ala Val Lys Gln
     130   135   140

Phe His Asp Ser Lys Ile Lys Phe Pro Leu Pro His Arg Val Leu Arg
145   150   155   160

Arg Gln His Lys Pro Arg Phe Thr Thr Lys Arg Pro Asn Thr Phe Phe
             165   170   175

<210>   2554
<211>   363
<212>   PRT
<213>   Homo sapiens

<400>   2554

Met Ala Leu His Cys Gln Glu Phe Gly Gly Lys Asn Tyr Glu Ala Ser
1   5   10   15

Met Ser His Val Asp Lys Phe Val Lys Glu Leu Leu Ser Ser Asp Ala
             20   25   30

Met Lys Glu Tyr Asn Arg Ala Arg Val Tyr Leu Asp Glu Asn Tyr Lys
         35   40   45

Ser Gln Glu His Phe Thr Ala Leu Gly Ser Phe Tyr Phe Leu His Glu
     50   55   60

Ser Leu Lys Asn Ile Tyr Gln Phe Asp Phe Lys Ala Lys Lys Tyr Arg
65   70   75   80

Lys Val Ala Gly Lys Glu Ile Tyr Ser Asp Thr Leu Glu Ser Thr Pro
                85   90   95

Met Leu Glu Lys Glu Lys Phe Arg Arg Leu Leu Pro Arg Val Gln Met
            100   105   110

Val Lys Lys Arg Leu His Pro Asp Glu Val Val Ile Ala Asp Cys Ala
            115   120   125

Phe Asp Leu Val Asn Ile His Leu Phe His Asp Ala Ser Asn Leu Val
    130   135   140

Ala Trp Glu Thr Ser Pro Ser Val Tyr Ser Gly Ile Arg His Lys Ala
145   150   155   160

Leu Gly Tyr Val Leu Asp Arg Ile Ile Asp Gln Arg Phe Glu Lys Val
            165   170   175

Ser Tyr Phe Val Phe Gly Asp Phe Asn Phe Arg Leu Asp Ser Lys Ser
            180   185   190

Val Val Glu Thr Leu Ser Ala Lys Pro Pro Met Gln Thr Val Arg Ala
    195   200   205

Ala Asp Thr Asn Glu Val Val Lys Leu Ile Phe Arg Glu Ser Asp Asn
    210   215   220

Asp Arg Lys Val Met Leu Gln Leu Glu Lys Lys Leu Phe Asp Tyr Phe
225   230   235   240

Asn Gln Glu Val Phe Arg Asp Asn Asn Gly Thr Ala Leu Leu Glu Phe
            245   250   255

Asp Lys Glu Leu Ser Val Phe Lys Asp Arg Leu Tyr Glu Leu Asp Ile
            260   265   270

Ser Phe Pro Pro Ser Tyr Pro Tyr Ser Glu Asp Ala Arg Gln Gly Glu
    275   280   285

Gln Tyr Met Asn Thr Arg Cys Pro Ala Trp Cys Asp Arg Ile Leu Met
    290   295   300

```
Ser Pro Ser Ala Lys Glu Leu Val Leu Arg Ser Glu Ser Glu Glu Lys
305             310             315             320


Val Val Thr Tyr Asp His Ile Gly Pro Asn Val Cys Met Gly Asp His
            325             330             335


Lys Pro Val Phe Leu Ala Phe Arg Ile Met Pro Gly Ala Gly Lys Pro
            340             345.            350


His Ala His Val His Lys Cys Cys Val Val Gln
        355             360
```

```
<210>  2555
<211>  56
<212>  PRT
<213>  Homo sapiens

<400>  2555
```

```
Met Gly His Gln Gln Leu Tyr Trp Ser His Pro Arg Lys Phe Gly Gln
1               5               10              15


Gly Ser Arg Ser Cys Arg Val Cys Ser Asn Arg His Gly Leu Ile Arg
            20              25              30


Lys Tyr Gly Leu Asn Met Cys Arg Gln Cys Phe Arg Gln Tyr Ala Lys
        35              40              45


Asp Ile Gly Phe Ile Lys Leu Asp
    50              55
```

```
<210>  2556
<211>  520
<212>  PRT
<213>  Homo sapiens

<400>  2556
```

```
Met Val Thr Ser Ser Phe Pro Ile Ser Val Ala Val Phe Ala Leu Ile
1               5               10              15


Thr Leu Gln Val Gly Thr Gln Asp Ser Phe Ile Ala Ala Val Tyr Glu
            20              25              30


His Ala Val Ile Leu Pro Asn Lys Thr Glu Thr Pro Val Ser Gln Glu
        35              40              45


Asp Ala Leu Asn Leu Met Asn Glu Asn Ile Asp Ile Leu Glu Thr Ala
    50              55              60
```

```
Ile Lys Gln Ala Ala Glu Gln Gly Ala Arg Ile Ile Val Thr Pro Glu
65              70              75              80


Asp Ala Leu Tyr Gly Trp Lys Phe Thr Arg Glu Thr Val Phe Pro Tyr
                85              90              95


Leu Glu Asp Ile Pro Asp Pro Gln Val Asn Trp Ile Pro Cys Gln Asp
            100             105             110


Pro His Arg Phe Gly His Thr Pro Val Gln Ala Arg Leu Ser Cys Leu
        115             120             125


Ala Lys Asp Asn Ser Ile Tyr Val Leu Ala Asn Leu Gly Asp Lys Lys
    130             135             140


Pro Cys Asn Ser Arg Asp Ser Thr Cys Pro Pro Asn Gly Tyr Phe Gln
145             150             155             160


Tyr Asn Thr Asn Val Val Tyr Asn Thr Glu Gly Lys Leu Val Ala Arg
                165             170             175


Tyr His Lys Tyr His Leu Tyr Ser Glu Pro Gln Phe Asn Val Pro Glu
            180             185             190


Lys Pro Glu Leu Val Thr Phe Asn Thr Ala Phe Gly Arg Phe Gly Ile
        195             200             205


Phe Thr Cys Phe Asp Ile Phe Phe Tyr Asp Pro Gly Val Thr Leu Val
    210             215             220


Lys Asp Phe His Val Asp Thr Ile Leu Phe Pro Thr Ala Trp Met Asn
225             230             235             240


Val Leu Pro Leu Leu Thr Ala Ile Glu Phe His Ser Ala Trp Ala Met
            245             250             255


Gly Met Gly Val Asn Leu Leu Val Ala Asn Thr His His Val Ser Leu
            260             265             270


Asn Met Thr Gly Ser Gly Ile Tyr Ala Pro Asn Gly Pro Lys Val Tyr
        275             280             285


His Tyr Asp Met Lys Thr Glu Leu Gly Lys Leu Leu Leu Ser Glu Val
    290             295             300
```

```
Asp Ser His Pro Leu Ser Ser Leu Ala Tyr Pro Thr Ala Val Asn Trp
305             310             315                 320

Asn Ala Tyr Ala Thr Thr Ile Lys Pro Phe Pro Val Gln Lys Asn Thr
            325             330                 335

Phe Arg Gly Phe Ile Ser Arg Asp Gly Phe Asn Phe Thr Glu Leu Phe
            340             345                 350

Glu Asn Ala Gly Asn Leu Thr Val Cys Gln Lys Glu Leu Cys Cys His
    355             360                 365

Leu Ser Tyr Arg Met Leu Gln Lys Glu Glu Asn Glu Val Tyr Val Leu
    370             375                 380

Gly Ala Phe Thr Gly Leu His Gly Arg Arg Arg Glu Tyr Trp Gln
385             390             395                 400

Val Cys Thr Met Leu Lys Cys Lys Thr Thr Asn Leu Thr Thr Cys Gly
            405             410                 415

Arg Pro Val Glu Thr Ala Ser Thr Arg Phe Glu Met Phe Ser Leu Ser
            420             425                 430

Gly Thr Phe Gly Thr Glu Tyr Val Phe Pro Glu Val Leu Leu Thr Glu
        435             440                 445

Ile His Leu Ser Pro Gly Lys Phe Glu Val Leu Lys Asp Gly Arg Leu
    450             455                 460

Val Asn Lys Asn Gly Ser Ser Gly Pro Ile Leu Thr Val Ser Leu Phe
465             470             475                 480

Gly Arg Trp Tyr Thr Lys Asp Ser Leu Tyr Ser Ser Cys Gly Thr Ser
            485             490                 495

Asn Ser Ala Ile Thr Tyr Leu Leu Ile Phe Ile Leu Leu Met Ile Ile
            500             505                 510

Ala Leu Gln Asn Ile Val Met Leu
            515             520
```

```
<210>  2557
<211>  564
<212>  PRT
<213>  Homo sapiens
```

<400> 2557

```
Met Ser Ala Gly Ser Ala Thr His Pro Gly Ala Gly Gly Arg Arg Ser
1               5                   10                  15

Lys Trp Asp Gln Pro Ala Pro Ala Pro Leu Leu Phe Leu Pro Pro Ala
            20                  25                  30

Ala Pro Gly Gly Glu Val Thr Ser Ser Gly Gly Ser Pro Gly Gly Thr
        35                  40                  45

Thr Ala Ala Pro Ser Gly Ala Leu Asp Ala Ala Ala Ala Val Ala Ala
    50                  55                  60

Lys Ile Asn Ala Met Leu Met Ala Lys Gly Lys Leu Lys Pro Thr Gln
65                  70                  75                  80

Asn Ala Ser Glu Lys Leu Gln Ala Pro Gly Lys Gly Leu Thr Ser Asn
                85                  90                  95

Lys Ser Lys Asp Asp Leu Val Val Ala Glu Val Glu Ile Asn Asp Val
            100                 105                 110

Pro Leu Thr Cys Arg Asn Leu Leu Thr Arg Gly Gln Thr Gln Asp Glu
        115                 120                 125

Ile Ser Arg Leu Ser Gly Ala Ala Val Ser Thr Arg Gly Arg Phe Met
    130                 135                 140

Thr Thr Glu Glu Lys Ala Lys Val Gly Pro Gly Asp Arg Pro Leu Tyr
145                 150                 155                 160

Leu His Val Gln Gly Gln Thr Arg Glu Leu Val Asp Arg Ala Val Asn
                165                 170                 175

Arg Ile Lys Glu Ile Ile Thr Asn Gly Val Val Lys Ala Ala Thr Gly
            180                 185                 190

Thr Ser Pro Thr Phe Asn Gly Ala Thr Val Thr Val Tyr His Gln Pro
        195                 200                 205

Ala Pro Ile Ala Gln Leu Ser Pro Ala Val Ser Gln Lys Pro Pro Phe
    210                 215                 220

Gln Ser Gly Met His Tyr Val Gln Asp Lys Leu Phe Val Gly Leu Glu
225                 230                 235                 240
```

942

His Ala Val Pro Thr Phe Asn Val Lys Glu Lys Val Glu Gly Pro Gly
                 245   250   255

Cys Ser Tyr Leu Gln His Ile Gln Ile Glu Thr Gly Ala Lys Val Phe
             260   265   270

Leu Arg Gly Lys Gly Ser Gly Cys Ile Glu Pro Ala Ser Gly Arg Glu
             275   280   285

Ala Phe Glu Pro Met Tyr Ile Tyr Ile Ser His Pro Lys Pro Glu Gly
     290   295   300

Leu Ala Ala Ala Lys Lys Leu Cys Glu Asn Leu Leu Gln Thr Val His
305   310   315   320

Ala Glu Tyr Ser Arg Phe Val Asn Gln Ile Asn Thr Ala Val Pro Leu
             325   330   335

Pro Gly Tyr Thr Gln Pro Ser Ala Ile Ser Ser Val Pro Pro Gln Pro
             340   345   350

Pro Tyr Tyr Pro Ser Asn Gly Tyr Gln Ser Gly Tyr Pro Val Val Pro
             355   360   365

Pro Pro Gln Gln Pro Val Gln Pro Pro Tyr Gly Val Pro Ser Ile Val
370   375   380

Pro Pro Ala Val Ser Leu Ala Pro Gly Val Leu Pro Ala Leu Pro Thr
385   390   395   400

Gly Val Pro Pro Val Pro Thr Gln Tyr Pro Ile Thr Gln Val Gln Pro
             405   410   415

Pro Ala Ser Thr Gly Gln Ser Pro Met Gly Gly Pro Phe Ile Pro Ala
             420   425   430

Ala Pro Val Lys Thr Ala Leu Pro Ala Gly Pro Gln Pro Gln Pro Gln
     435   440   445

Pro Gln Pro Pro Leu Pro Ser Gln Pro Gln Ala Gln Lys Arg Arg Phe
     450   455   460

Thr Glu Glu Leu Pro Asp Glu Arg Glu Ser Gly Leu Leu Gly Tyr Gln
465   470   475   480

His Gly Pro Ile His Met Thr Asn Leu Gly Thr Gly Phe Ser Ser Gln
            485   490   495

Asn Glu Ile Glu Gly Ala Gly Ser Lys Pro Ala Ser Ser Ser Gly Lys
            500   505   510

Glu Arg Glu Arg Asp Arg Gln Leu Met Pro Pro Pro Ala Phe Pro Val
            515   520   .   525

Thr Gly Ile Lys Thr Glu Ser Asp Glu Arg Asn Gly Ser Gly Thr Leu
            530   535   540

Thr Gly Ser His Gly Glu Cys Asp Ile Ala Gly Gly Thr Gly Glu Trp
545   550   555   560

Leu Arg Leu Val

<210>   2558
<211>   462
<212>   PRT
<213>   Homo sapiens

<400>   2558

Met Gly Lys Glu Lys Thr His Ile Asn Ile Val Val Ile Gly His Val
1   5   10   15

Asp Ser Gly Lys Ser Thr Thr Thr Gly His Leu Ile Tyr Lys Cys Gly
            20   .   25   30

Gly Ile Asp Lys Arg Thr Ile Glu Lys Phe Glu Lys Glu Ala Ala Glu
            35   40   45

Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys
            50   55   60

Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe
65   70   75   80

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg
            85   90   95

Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala
            100   105   110

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser

944

                    115   120   125

    Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly
        130   135   140

    Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro
        145   150   155   160

    Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr
                    165   170   175

    Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro
                180   185   190

    Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met
                195   200   205

    Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser
        210   215   220

    Gly Thr Thr Leu Leu Glu Ala Leu Asp Cys Ile Leu Pro Pro Thr Arg
    225   230   235   240

    Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile
                245   250   255

    Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu
                260   265   270

    Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu
        275   280   285

    Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro
        290   295   300

    Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val
    305   310   315   320

    Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu
                    325   330   335

    Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln
                340   345   350

    Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile
                355   360   365

```
Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly
    370             375             380

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala
385             390             395                 400

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser
            405             410                 415

Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr
        420             425             430

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala
        435             440             445

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys
    450             455             460
```

<210> 2559
<211> 394
<212> PRT
<213> Homo sapiens

<400> 2559

```
Met Ser Gly Glu Asp Glu Gln Gln Glu Gln Thr Ile Ala Glu Asp Leu
1               5               10                  15

Val Val Thr Lys Tyr Lys Met Gly Gly Asp Ile Ala Asn Arg Val Leu
            20              25                  30

Arg Ser Leu Val Glu Ala Ser Ser Ser Gly Val Ser Val Leu Ser Leu
        35              40                  45

Cys Glu Lys Gly Asp Ala Met Ile Met Glu Glu Thr Gly Lys Ile Phe
    50              55                  60

Lys Lys Glu Lys Glu Met Lys Lys Gly Ile Ala Phe Pro Thr Ser Ile
65              70                  75                  80

Ser Val Asn Asn Cys Val Cys His Phe Ser Pro Leu Lys Ser Asp Gln
                85              90                  95

Asp Tyr Ile Leu Lys Glu Gly Asp Leu Val Lys Ile Asp Leu Gly Val
        100             105                 110
```

His Val Asp Gly Phe Ile Ala Asn Val Ala His Thr Phe Val Val Asp
         115   120   125

Val Ala Gln Gly Thr Gln Val Thr Gly Arg Lys Ala Asp Val Ile Lys
    130   135   140

Ala Ala His Leu Cys Ala Glu Ala Ala Leu Arg Leu Val Lys Pro Gly
145   150   155   160

Asn Gln Asn Thr Gln Val Thr Glu Ala Trp Asn Lys Val Ala His Ser
             165   170   175

Phe Asn Cys Thr Pro Ile Glu Gly Met Leu Ser His Gln Leu Lys Gln
             180   185   190

His Val Ile Asp Gly Glu Lys Thr Ile Ile Gln Asn Pro Thr Asp Gln
         195   200   205

Gln Lys Lys Asp His Glu Lys Ala Glu Phe Glu Val His Glu Val Tyr
    210   215   220

Ala Val Asp Val Leu Val Ser Ser Gly Glu Gly Lys Ala Lys Asp Ala
225   230   235   240

Gly Gln Arg Thr Thr Ile Tyr Lys Arg Asp Pro Ser Lys Gln Tyr Gly
             245   250   255

Leu Lys Met Lys Thr Ser Arg Ala Phe Phe Ser Glu Val Glu Arg Arg
         260   265   270

Phe Asp Ala Met Pro Phe Thr Leu Arg Ala Phe Glu Asp Glu Lys Lys
    275   280   285

Ala Arg Met Gly Val Val Glu Cys Ala Lys His Glu Leu Leu Gln Pro
    290   295   300

Phe Asn Val Leu Tyr Glu Lys Glu Gly Glu Phe Val Ala Gln Phe Lys
305   310   315   320

Phe Thr Val Leu Leu Met Pro Asn Gly Pro Met Arg Ile Thr Ser Gly
         325   330   335

Pro Phe Glu Pro Asp Leu Tyr Lys Ser Glu Met Glu Val Gln Asp Ala
         340   345   350

Glu Leu Lys Ala Leu Leu Gln Ser Ser Ala Ser Arg Lys Thr Gln Lys

```
         355                   360                   365
```

Lys Lys Lys Lys Lys Ala Ser Lys Thr Ala Glu Asn Pro Thr Ser Gly
    370   375   380

Glu Thr Leu Glu Glu Asn Glu Ala Gly Asp
385   390

```
<210>   2560
<211>   335
<212>   PRT
<213>   Homo sapiens

<400>   2560
```

Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg
1   5   10   15

Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala
            20   25   30

Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln
        35   40   45

Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Lys Ala Glu Asn
    50   55   60

Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg
65   70   75   80

Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val
            85   90   95

Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
            100   105   110

Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
        115   120   125

Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
    130   135   140

Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
145   150   155   160

Ala Lys Val Ile His Asp Asn Phe Gly Ile Val Glu Gly Leu Met Thr
            165   170   175

```
Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
            180                 185                 190

Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
        195                 200                 205

Ala Ser Thr Gly Ala Ala Lys Ala Val Gly Lys Val Ile Pro Glu Leu
    210                 215                 220

Asn Gly Lys Leu Thr Gly Met Ala Phe Arg Val Pro Thr Ala Asn Val
225                 230                 235                 240

Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
            245                 250                 255

Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
            260                 265                 270

Ile Leu Gly Tyr Thr Glu His Gln Val Val Ser Ser Asp Phe Asn Ser
            275                 280                 285

Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
    290                 295                 300

Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
305                 310                 315                 320

Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
            325                 330                 335
```

<210> 2561
<211> 1912
<212> PRT
<213> Homo sapiens

<400> 2561

```
Met Ala Ser Gly Leu Gly Ser Pro Ser Pro Cys Ser Ala Gly Ser Glu
1               5                   10                  15

Glu Glu Asp Met Asp Ala Leu Leu Asn Asn Ser Leu Pro Pro Pro His
            20                  25                  30

Pro Glu Asn Glu Glu Asp Pro Glu Glu Asp Leu Ser Glu Thr Glu Thr
        35                  40                  45

Pro Lys Leu Lys Lys Lys Lys Lys Pro Lys Lys Pro Arg Asp Pro Lys
```

```
        50                      55                      60        ·


Ile Pro Lys Ser Lys Arg Gln Lys Lys Glu Arg Met Leu Leu Cys Arg
65                  70                  75                  80


Gln Leu Gly Asp Ser Ser Gly Glu Gly Pro Glu Phe Val Glu Glu Glu
                85                  90                  95


Glu Glu Val Ala Leu Arg Ser Asp Ser Glu Gly Ser Asp Tyr Thr Pro
            100                 105                 110


Gly Lys Lys Lys Lys Lys Lys Leu Gly Pro Lys Lys Glu Lys Lys Ser
        115                 120                 125


Lys Ser Lys Arg Lys Glu Glu Glu Glu Glu Asp Asp Asp Asp Asp Asp
    130                 135                 140


Ser Lys Glu Pro Lys Ser Ser Ala Gln Leu Leu Glu Asp Trp Gly Met
145                 150                 155                 160


Glu Asp Ile Asp His Val Phe Ser Glu Glu Asp Tyr Arg Thr Leu Thr
            165                 170                 175


Asn Tyr Lys Ala Phe Ser Gln Phe Val Arg Pro Leu Ile Ala Ala Lys
        180                 185                 190


Asn Pro Lys Ile Ala Val Ser Lys Met Met Met Val Leu Gly Ala Lys
        195                 200                 205


Trp Arg Glu Phe Ser Thr Asn Asn Pro Phe Lys Gly Ser Ser Gly Ala
    210                 215                 220


Ser Val Ala Ala Ala Ala Ala Ala Val Ala Val Val Glu Ser Met
225                 230                 235                 240


Val Thr Ala Thr Glu Val Ala Pro Pro Pro Pro Val Glu Val Pro
            245                 250                 255


Ile Arg Lys Ala Lys Thr Lys Glu Gly Lys Gly Pro Asn Ala Arg Arg
        260                 265                 270


Lys Pro Lys Gly Ser Pro Arg Val Pro Asp Ala Lys Lys Pro Lys Pro
        275                 280                 285


Lys Lys Val Ala Pro Leu Lys Ile Lys Leu Gly Gly Phe Gly Ser Lys
        290                 295                 300
```

Arg Lys Arg Ser Ser Ser Glu Asp Asp Asp Leu Asp Val Glu Ser Asp
305   310   315   320

Phe Asp Asp Ala Ser Ile Asn Ser Tyr Ser Val Ser Asp Gly Ser Thr
                325   330   335

Ser Arg Ser Ser Arg Ser Arg Lys Lys Leu Arg Thr Thr Lys Lys Lys
                340   345   350

Lys Lys Gly Glu Glu Glu Val Thr Ala Val Asp Gly Tyr Glu Thr Asp
                355   360   365

His Gln Asp Tyr Cys Glu Val Cys Gln Gln Gly Gly Glu Ile Ile Leu
    370   375   380

Cys Asp Thr Cys Pro Arg Ala Tyr His Met Val Cys Leu Asp Pro Asp
385   390   395   400

Met Glu Lys Ala Pro Glu Gly Lys Trp Ser Cys Pro His Cys Glu Lys
                405   410   415

Glu Gly Ile Gln Trp Glu Ala Lys Glu Asp Asn Ser Glu Gly Glu Glu
                420   425   430

Ile Leu Glu Glu Val Gly Gly Asp Leu Glu Glu Glu Asp Asp His His
    435   440   445

Met Glu Phe Cys Arg Val Cys Lys Asp Gly Gly Glu Leu Leu Cys Cys
    450   455   460

Asp Thr Cys Pro Ser Ser Tyr His Ile His Cys Leu Asn Pro Pro Leu
465   470   475   480

Pro Glu Ile Pro Asn Gly Glu Trp Leu Cys Pro Arg Cys Thr Cys Pro
                485   490   495

Ala Leu Lys Gly Lys Val Gln Lys Ile Leu Ile Trp Lys Trp Gly Gln
                500   505   510

Pro Pro Ser Pro Thr Pro Val Pro Arg Pro Pro Asp Ala Asp Pro Asn
                515   520   525

Thr Pro Ser Pro Lys Pro Leu Glu Gly Arg Pro Glu Arg Gln Phe Phe
    530   535   540

951

Val Lys Trp Gln Gly Met Ser Tyr Trp His Cys Ser Trp Val Ser Glu
545   550   555   560

Leu Gln Leu Glu Leu His Cys Gln Val Met Phe Arg Asn Tyr Gln Arg
                565   570   575

Lys Asn Asp Met Asp Glu Pro Pro Ser Gly Asp Phe Gly Gly Asp Glu
                580   585   590

Glu Lys Ser Arg Lys Arg Lys Asn Lys Asp Pro Lys Phe Ala Glu Met
                595   600   605

Glu Glu Arg Phe Tyr Arg Tyr Gly Ile Lys Pro Glu Trp Met Met Ile
        610   615   620

His Arg Ile Leu Asn His Ser Val Asp Lys Lys Gly His Val His Tyr
625   630   635   640

Leu Ile Lys Trp Arg Asp Leu Pro Tyr Asp Gln Ala Ser Trp Glu Ser
                645   650   655

Glu Asp Val Glu Ile Gln Asp Tyr Asp Leu Phe Lys Gln Ser Tyr Trp
                660   665   670

Asn His Arg Glu Leu Met Arg Gly Glu Glu Gly Arg Pro Gly Lys Lys
                675   680   685

Leu Lys Lys Val Lys Leu Arg Lys Leu Glu Arg Pro Pro Glu Thr Pro
        690   695   700

Thr Val Asp Pro Thr Val Lys Tyr Glu Arg Gln Pro Glu Tyr Leu Asp
705   710   715   720

Ala Thr Gly Gly Thr Leu His Pro Tyr Gln Met Glu Gly Leu Asn Trp
                725   730   735

Leu Arg Phe Ser Trp Ala Gln Gly Thr Asp Thr Ile Leu Ala Asp Glu
                740   745   750

Met Gly Leu Gly Lys Thr Val Gln Thr Ala Val Phe Leu Tyr Ser Leu
        755   760   765

Tyr Lys Glu Gly His Ser Lys Gly Pro Phe Leu Val Ser Ala Pro Leu
        770   775   780

952

Ser Thr Ile Ile Asn Trp Glu Arg Glu Phe Glu Met Trp Ala Pro Asp
785   790   795   800

Met Tyr Val Val Thr Tyr Val Gly Asp Lys Asp Ser Arg Ala Ile Ile
                805   810   815

Arg Glu Asn Glu Phe Ser Phe Glu Asp Asn Ala Ile Arg Gly Gly Lys
            820   825   830

Lys Ala Ser Arg Met Lys Lys Glu Ala Ser Val Lys Phe His Val Leu
            835   840   845

Leu Thr Ser Tyr Glu Leu Ile Thr Ile Asp Met Ala Ile Leu Gly Ser
    850   855   860

Ile Asp Trp Ala Cys Leu Ile Val Asp Glu Ala His Arg Leu Lys Asn
865   870   875   880

Asn Gln Ser Lys Phe Phe Arg Val Leu Asn Gly Tyr Ser Leu Gln His
            885   890   895

Lys Leu Leu Leu Thr Gly Thr Pro Leu Gln Asn Asn Leu Glu Glu Leu
        900   905   910

Phe His Leu Leu Asn Phe Leu Thr Pro Glu Arg Phe His Asn Leu Glu
    915   920   925

Gly Phe Leu Glu Glu Phe Ala Asp Ile Ala Lys Glu Asp Gln Ile Lys
    930   935   940

Lys Leu His Asp Met Leu Gly Pro His Met Leu Arg Arg Leu Lys Ala
945   950   955   960

Asp Val Phe Lys Asn Met Pro Ser Lys Thr Glu Leu Ile Val Arg Val
                965   970   975

Glu Leu Ser Pro Met Gln Lys Lys Tyr Tyr Lys Tyr Ile Leu Thr Arg
        980   985   990

Asn Phe Glu Ala Leu Asn Ala Arg Gly Gly Gly Asn Gln Val Ser Leu
        995   1000   1005

Leu Asn Val Val Met Asp Leu Lys Lys Cys Cys Asn His Pro Tyr
    1010   1015   1020

Leu Phe Pro Val Ala Ala Met Glu Ala Pro Lys Met Pro Asn Gly

953

```
    1025              1030              1035


Met Tyr  Asp Gly Ser Ala Leu  Ile Arg Ala Ser Gly  Lys Leu Leu
    1040              1045              1050


Leu Leu  Gln Lys Met Leu Lys  Asn Leu Lys Glu Gly  Gly His Arg
    1055              1060              1065


Val Leu  Ile Phe Ser Gln Met  Thr Lys Met Leu Asp  Leu Leu Glu
    1070              1075              1080


Asp Phe  Leu Glu·His Glu Gly  Tyr Lys Tyr Glu Arg  Ile Asp Gly
    1085              1090              1095


Gly Ile  Thr Gly Asn Met Arg  Gln Glu Ala Ile Asp  Arg Phe Asn
    1100              1105              1110


Ala Pro  Gly Ala Gln Gln Phe  Cys Phe Leu Leu Ser  Thr Arg Ala
    1115              1120  ·  .           1125


Gly Gly  Leu Gly Ile Asn Leu  Ala Thr Ala Asp Thr  Val Ile Ile
    1130              1135              1140
                                          .

Tyr Asp  Ser Asp Trp Asn Pro  His Asn Asp Ile Gln  Ala Phe Ser
    1145              1150              1155


Arg Ala  His Arg Ile Gly Gln  Asn Lys Lys Val Met  Ile Tyr Arg
    1160              1165              1170


Phe Val  Thr Arg Ala Ser Val  Glu Glu Arg Ile Thr  Gln Val Ala
    1175              1180              1185


Lys Lys  Lys Met Met Leu Thr  His Leu Val Val Arg  Pro Gly Leu
    1190              1195              1200


Gly Ser  Lys Thr Gly Ser Met  Ser Lys Gln Glu Leu  Asp Asp Ile
    1205              1210              1215


Leu Lys  Phe Gly Thr Glu Glu  Leu Phe Lys Asp Glu  Ala Thr Asp
    1220              1225              1230


Gly Gly  Gly Asp Asn Lys Glu  Gly Glu Asp Ser Ser  Val Ile His
    1235              1240              1245


Tyr Asp  Asp Lys Ala Ile Glu  Arg Leu Leu Asp Arg  Asn Gln Asp
    1250              1255              1260
```

954

Glu Thr Glu Asp Thr Glu Leu Gln Gly Met Asn Glu Tyr Leu Ser
    1265   1270   1275

Ser Phe Lys Val Ala Gln Tyr Val Val Arg Glu Glu Glu Met Gly
    1280   1285   1290

Glu Glu Glu Glu Val Glu Arg Glu Ile Ile Lys Gln Glu Glu Ser
    1295   1300   1305

Val Asp Pro Asp Tyr Trp Glu Lys Leu Leu Arg His His Tyr Glu
    1310   1315   1320

Gln Gln Gln Glu Asp Leu Ala Arg Asn Leu Gly Lys Gly Lys Arg
    1325   1330   1335

Ile Arg Lys Gln Val Asn Tyr Asn Asp Gly Ser Gln Glu Asp Arg
    1340   1345   1350

Asp Trp Gln Asp Asp Gln Ser Asp Asn Gln Ser Asp Tyr Ser Val
    1355   1360   1365

Ala Ser Glu Glu Gly Asp Glu Asp Phe Asp Glu Arg Ser Glu Ala
    1370   1375   1380

Pro Arg Arg Pro Ser Arg Lys Gly Leu Arg Asn Asp Lys Asp Lys
    1385   1390   1395

Pro Leu Pro Pro Leu Leu Ala Arg Val Gly Gly Asn Ile Glu Val
    1400   1405   1410

Leu Gly Phe Asn Ala Arg Gln Arg Lys Ala Phe Leu Asn Ala Ile
    1415   1420   1425

Met Arg Tyr Gly Met Pro Pro Gln Asp Ala Phe Thr Thr Gln Trp
    1430   1435   1440

Leu Val Arg Asp Leu Arg Gly Lys Ser Glu Lys Glu Phe Lys Ala
    1445   1450   1455

Tyr Val Ser Leu Phe Met Arg His Leu Cys Glu Pro Gly Ala Asp
    1460   1465   1470

Gly Ala Glu Thr Phe Ala Asp Gly Val Pro Arg Glu Gly Leu Ser
    1475   1480   1485

```
Arg Gln  His Val Leu Thr Arg  Ile Gly Val Met Ser  Leu Ile Arg
    1490                  1495              1500

Lys Lys  Val Gln Glu Phe Glu  His Val Asn Gly Arg  Trp Ser Met
    1505                  1510              1515

Pro Glu  Leu Ala Glu Val Glu  Glu Asn Lys Lys Met  Ser Gln Pro
    1520                  1525              1530

Gly Ser  Pro Ser Pro Lys Thr  Pro Thr Pro Ser Thr  Pro Gly Asp
    1535                  1540              1545

Thr Gln  Pro Asn Thr Pro Ala  Pro Val Pro Pro Ala  Glu Asp Gly
    1550                  1555              1560

Ile Lys  Ile Glu Glu Asn Ser  Leu Lys Glu Glu Glu  Ser Ile Glu
    1565                  1570              1575

Gly Glu  Lys Glu Val Lys Ser  Thr Ala Pro Glu Thr  Ala Ile Glu
    1580                  1585              1590

Cys Thr  Gln Ala Pro Ala Pro  Ala Ser Glu Asp Glu  Lys Val Val
    1595                  1600              1605

Val Glu  Pro Pro Glu Gly Glu  Glu Lys Val Glu Lys  Ala Glu Val
    1610                  1615              1620

Lys Glu  Arg Thr Glu Glu Pro  Met Glu Thr Glu Pro  Lys Gly Ala
    1625                  1630              1635

Ala Asp  Val Glu Lys Val Glu  Glu Lys Ser Ala Ile  Asp Leu Thr
    1640                  1645              1650

Pro Ile  Val Val Glu Asp Lys  Glu Glu Lys Lys Glu  Glu Glu Glu
    1655                  1660              1665

Lys Lys  Glu Val Met Leu Gln  Asn Gly Glu Thr Pro  Lys Asp Leu
    1670                  1675              1680

Asn Asp  Glu Lys Gln Lys Lys  Asn Ile Lys Gln Arg  Phe Met Phe
    1685                  1690              1695

Asn Ile  Ala Asp Gly Gly Phe  Thr Glu Leu His Ser  Leu Trp Gln
    1700                  1705              1710
```

```
Asn Glu  Glu Arg Ala Ala Thr  Val Thr Lys Lys Thr  Tyr Glu Ile
    1715                 1720                 1725


Trp His  Arg Arg His Asp Tyr  Trp Leu Leu Ala Gly  Ile Ile Asn
    1730                 1735                 1740


His Gly  Tyr Ala Arg Trp Gln  Asp Ile Gln Asn Asp  Pro Arg Tyr
    1745                 1750                 1755


Ala Ile  Leu Asn Glu Pro Phe  Lys Gly Glu Met Asn  Arg Gly Asn
    1760                 1765                 1770


Phe Leu  Glu Ile Lys Asn Lys  Phe Leu Ala Arg Arg  Phe Lys Leu
    1775                 1780                 1785


Leu Glu  Gln Ala Leu Val Ile  Glu Glu Gln Leu Arg  Arg Ala Ala
    1790                 1795                 1800


Tyr Leu  Asn Met Ser Glu Asp  Pro Ser His Pro Ser  Met Ala Leu
    1805                 1810                 1815


Asn Thr  Arg Phe Ala Glu Val  Glu Cys Leu Ala Glu  Ser His Gln
    1820                 1825                 1830


His Leu  Ser Lys Glu Ser Met  Ala Gly Asn Lys Pro  Ala Asn Ala
    1835                 1840                 1845


Val Leu  His Lys Val Leu Lys  Gln Leu Glu Glu Leu  Leu Ser Asp
    1850                 1855                 1860


Met Lys  Ala Asp Val Thr Arg  Leu Pro Ala Thr Ile  Ala Arg Ile
    1865                 1870                 1875


Pro Pro  Val Ala Val Arg Leu  Gln Met Ser Glu Arg  Asn Ile Leu
    1880                 1885                 1890


Ser Arg  Leu Ala Asn Arg Ala  Pro Glu Pro Thr Pro  Gln Gln Val
    1895                 1900                 1905


Ala Gln  Gln Gln
    1910


<210>   2562
<211>   345
<212>   PRT
<213>   Homo sapiens
```

<400> 2562

```
Met Pro Gln Arg Pro Ala Ala Ser Asn Ile Pro Val Val Gly Ser Pro
1               5                   10                  15

Asn Pro Pro Ser Thr His Phe Ala Ser Gln Asn Gln His Ser Tyr Ser
            20                  25                  30

Ser Pro Pro Trp Ala Gly Gln His Asn Arg Lys Gly Glu Lys Asn Gly
        35                  40                  45

Met Gly Leu Cys Arg Leu Ser Met Lys Val Trp Glu Thr Val Gln Arg
    50                  55                  60

Lys Gly Thr Thr Ser Cys Gln Glu Val Val Gly Glu Leu Val Ala Lys
65                  70                  75                  80

Phe Arg Ala Ala Ser Asn His Ala Ser Pro Asn Glu Ser Ala Tyr Asp
                85                  90                  95

Val Lys Asn Ile Lys Arg Arg Thr Tyr Asp Ala Leu Asn Val Leu Met
            100                 105                 110

Ala Met Asn Ile Ile Ser Arg Glu Lys Lys Lys Ile Lys Trp Ile Gly
        115                 120                 125

Leu Thr Thr Asn Ser Ala Gln Asn Cys Gln Asn Leu Arg Val Glu Arg
    130                 135                 140

Gln Lys Arg Leu Glu Arg Ile Lys Gln Lys Gln Ser Glu Leu Gln Gln
145                 150                 155                 160

Leu Ile Leu Gln Gln Ile Ala Phe Lys Asn Leu Val Leu Arg Asn Gln
                165                 170                 175

Tyr Val Glu Glu Gln Val Ser Gln Arg Pro Leu Pro Asn Ser Val Ile
            180                 185                 190

His Val Pro Phe Ile Ile Ile Ser Ser Ser Lys Lys Thr Val Ile Asn
        195                 200                 205

Cys Ser Ile Ser Asp Asp Lys Ser Glu Tyr Leu Phe Lys Phe Asn Ser
    210                 215                 220

Ser Phe Glu Ile His Asp Asp Thr Glu Val Leu Met Trp Met Gly Met
225                 230                 235                 240
```

```
Thr Phe Gly Leu Glu Ser Gly Ser Cys Ser Ala Glu Asp Leu Lys Met
            245                 250                 255

Ala Arg Asn Leu Val Pro Lys Ala Leu Glu Pro Tyr Val Thr Glu Met
            260                 265                 270

Ala Gln Gly Thr Phe Gly Gly Val Phe Thr Thr Ala Gly Ser Arg Ser
        275                 280                 285

Asn Gly Thr Trp Leu Ser Ala Ser Asp Leu Thr Asn Ile Ala Ile Gly
    290                 295                 300

Met Leu Ala Thr Ser Ser Gly Gly Ser Gln Tyr Ser Gly Ser Arg Val
305                 310                 315                 320

Glu Thr Pro Ala Val Glu Glu Glu Glu Glu Asp Asn Asn Asp Asp
            325                 330                 335

Asp Leu Ser Glu Asn Asp Glu Asp Asp
            340                 345
```

```
<210> 2563
<211> 553
<212> PRT
<213> Homo sapiens

<400> 2563
```

```
Met Ser Thr Glu Thr Glu Leu Gln Val Ala Val Lys Thr Ser Ala Lys
1               5                   10                  15

Lys Asp Ser Arg Lys Lys Gly Gln Asp Arg Ser Glu Ala Thr Leu Ile
            20                  25                  30

Lys Arg Phe Lys Gly Glu Gly Val Arg Tyr Lys Ala Lys Leu Ile Gly
        35                  40                  45

Ile Asp Glu Val Ser Ala Ala Arg Gly Asp Lys Leu Cys Gln Asp Ser
    50                  55                  60

Met Met Lys Leu Lys Gly Val Val Ala Gly Ala Arg Ser Lys Gly Glu
65                  70                  75                  80

His Lys Gln Lys Ile Phe Leu Thr Ile Ser Phe Gly Gly Ile Lys Ile
                85                  90                  95

Phe Asp Glu Lys Thr Gly Ala Leu Gln His His His Ala Val His Glu
```

```
              100                    105                    110
```

```
      Ile Ser Tyr Ile Ala Lys Asp Ile Thr Asp His Arg Ala Phe Gly Tyr
              115                    120                    125
```

```
      Val Cys Gly Lys Glu Gly Asn His Arg Phe Val Ala Ile Lys Thr Ala
              130                    135                    140
```

```
      Gln Ala Ala Glu Pro Val Ile Leu Asp Leu Arg Asp Leu Phe Gln Leu
      145                    150                    155                    160
```

```
      Ile Tyr Glu Leu Lys Gln Arg Glu Glu Leu Glu Lys Lys Ala Gln Lys
                      165                    170                    175
```

```
      Asp Lys Gln Cys Glu Gln Ala Val Tyr Gln Thr Ile Leu Glu Glu Asp
                      180                    185                    190
```

```
      Val Glu Asp Pro Val Tyr Gln Tyr Ile Val Phe Glu Ala Gly His Glu
              195                    200                    205
```

```
      Pro Ile Arg Asp Pro Glu Thr Glu Glu Asn Ile Tyr Gln Val Pro Thr
              210                    215                    220
```

```
      Ser Gln Lys Lys Glu Gly Val Tyr Asp Val Pro Lys Ser Gln Pro Ala
      225                    230                    235                    240
```

```
      Val Thr Gln Leu Glu Leu Phe Gly Asp Met Ser Thr Pro Pro Asp Ile
                      245                    250                    255
```

```
      Thr Ser Pro Pro Thr Pro Ala Thr Pro Gly Asp Ala Phe Ile Pro Ser
                      260                    265                    270
```

```
      Ser Ser Gln Thr Leu Pro Ala Ser Ala Asp Val Phe Ser Ser Val Pro
              275                    280                    285
```

```
      Phe Gly Thr Ala Ala Val Pro Ser Gly Tyr Val Ala Met Gly Ala Val
      290                    295                    300
```

```
      Leu Pro Ser Phe Trp Gly Gln Gln Pro Leu Val Gln Gln Gln Met Val
      305                    310                    315                    320
```

```
      Met Gly Ala Gln Pro Pro Val Ala Gln Val Met Pro Gly Ala Gln Pro
                      325                    330                    335
```

```
      Ile Ala Trp Gly Gln Pro Gly Leu Phe Pro Ala Thr Gln Gln Pro Trp
              340                    345                    350
```

```
Pro Thr Val Ala Gly Gln Phe Pro Pro Ala Ala Phe Met Pro Thr Gln
        355                 360                 365

Thr Val Met Pro Leu Pro Ala Ala Met Phe Gln Gly Pro Leu Thr Pro
    370                 375                 380

Leu Ala Thr Val Pro Gly Thr Ser Asp Ser Thr Arg Ser Ser Pro Gln
385                 390                 395                 400

Thr Asp Lys Pro Arg Gln Lys Met Gly Lys Glu Thr Phe Lys Asp Phe
                405                 410                 415

Gln Met Ala Gln Pro Pro Pro Val Pro Ser Arg Lys Pro Asp Gln Pro
            420             425                 430

Ser Leu Thr Cys Thr Ser Glu Ala Phe Ser Ser Tyr Phe Asn Lys Val
        435                 440                 445

Gly Val Ala Gln Asp Thr Asp Asp Cys Asp Asp Phe Asp Ile Ser Gln
    450                 455                 460

Leu Asn Leu Thr Pro Val Thr Ser Thr Thr Pro Ser Thr Asn Ser Pro
465                 470                 475                 480

Pro Thr Pro Ala Pro Arg Gln Ser Ser Pro Ser Lys Ser Ser Ala Ser
            485                 490                 495

His Ala Ser Asp Pro Thr Thr Asp Asp Ile Phe Glu Glu Gly Phe Glu
            500                 505                 510

Ser Pro Ser Lys Ser Glu Glu Gln Glu Ala Pro Asp Gly Ser Gln Ala
        515                 520                 525

Ser Ser Asn Ser Asp Pro Phe Gly Glu Pro Ser Gly Glu Pro Ser Gly
        530                 535                 540

Asp Asn Ile Ser Pro Gln Ala Gly Ser
545                 550
```

<210> 2564
<211> 1336
<212> PRT
<213> Homo sapiens

<400> 2564

```
Met Glu Asn Leu Pro Ala Val Thr Thr Glu Glu Pro Thr Pro Met Gly
1               5                   10                  15

Arg Gly Pro Val Gly Pro Ser Gly Gly Gly Ser Thr Arg Asp Gln Val
            20              25                  30

Arg Thr Val Val Met Arg Pro Ser Val Ser Trp Glu Lys Ala Gly Pro
        35              40                  45

Glu Glu Ala Lys Ala Pro Val Arg Gly Asp Glu Ala Pro Pro Ala Arg
    50              55                  60

Val Ala Gly Pro Ala Ala Gly Thr Pro Pro Cys Gln Met Gly Val Tyr
65              70              75                  80

Pro Thr Asp Leu Thr Leu Gln Leu Leu Ala Val Arg Arg Lys Ser Arg
            85                  90                  95

Leu Arg Asp Pro Gly Leu Gln Gln Thr Leu Arg Gly Gln Leu Arg Leu
            100             105             110

Leu Glu Asn Asp Ser Arg Glu Met Ala Arg Val Leu Gly Glu Leu Ser
    115             120             125

Ala Arg Leu Leu Ser Ile His Ser Asp Gln Asp Arg Ile Val Val Thr
    130             135             140

Phe Lys Thr Phe Glu Glu Ile Trp Lys Phe Ser Thr Tyr His Ala Leu
145             150             155             160

Gly Phe Thr His His Cys Leu Ala Asn Leu Leu Met Asp Gln Ala Phe
            165             170             175

Trp Leu Leu Leu Pro Ser Glu Glu Glu Thr Ala Ile Gln Val His
            180             185             190

Val Asp Glu Asn Ala Leu Arg Leu Thr His Glu Ser Leu Leu Ile Gln
    195             200             205

Glu Gly Pro Phe Phe Val Leu Cys Pro Asp His His Val Arg Val Met
    210             215             220

Thr Gly Pro Arg Asp Ala Gly Asn Gly Pro Gln Ala Leu Arg Gln Ala
225             230             235             240

Ser Gly Ala Pro Gln Gly Glu Ala Ala Pro Glu Thr Asp Ser Ser Pro
```

962

<pre>
                  245   250   255

  Pro Ser Pro Ser Val Ser Ser Glu Glu Val Ala Val Ala Ala Ala Pro
              260   265   270

  Glu Pro Leu Ile Pro Phe His Gln Trp Ala Leu Arg Ile Pro Gln Asp
              275   280   285

  Pro Ile Asp Asp Ala Met Gly Gly Pro Val Met Pro Gly Asn Pro Leu
          290   295   300

  Met Ala Val Gly Leu Ala Ser Ala Leu Ala Asp Phe Gln Gly Ser Gly
  305   310   315   320

  Pro Glu Glu Met Thr Phe Arg Gly Gly Asp Leu Ile Glu Ile Leu Gly
              325   330   335

  Ala Gln Val Pro Ser Leu Pro Trp Cys Val Gly Arg His Ala Ala Ser
              340   345   350

  Gly Arg Val Gly Phe Val Arg Ser Ser Leu Ile Ser Met Gln Gly Pro
              355   360   365

  Val Ser Glu Leu Glu Ser Ala Ile Phe Leu Asn Glu Glu Glu Lys Ser
      370   375   380

  Phe Phe Ser Glu Gly Cys Phe Ser Glu Glu Asp Ala Arg Gln Leu Leu
  385   390   395   400

  Arg Arg Met Ser Gly Thr Asp Val Cys Ser Val Tyr Ser Leu Asp Ser
              405   410   415

  Val Glu Glu Ala Glu Thr Glu Gln Pro Gln Glu Lys Glu Ile Pro Pro
              420   425   430

  Pro Cys Leu Ser Pro Glu Pro Gln Glu Thr Leu Gln Lys Val Lys Asn
              435   440   445

  Val Leu Glu Gln Cys Lys Thr Cys Pro Gly Cys Pro Gln Glu Pro Ala
      450   455   460

  Ser Trp Gly Leu Cys Ala Ala Ser Ser Asp Val Ser Leu Gln Asp Pro
  465   470   475   480

  Glu Glu Pro Ser Phe Cys Leu Glu Ala Glu Asp Asp Trp Glu Asp Pro
              485   490   495
</pre>

963

Glu Ala Leu Ser Ser Leu Leu Leu Phe Leu Asn Ala Pro Gly Tyr Lys
                500   505   510

Ala Ser Phe Arg Gly Leu Tyr Asp Val Ala Leu Pro Trp Leu Ser Ser
            515   520   525

Val Phe Arg Ser Phe Ser Asp Glu Glu Glu Leu Thr Gly Arg Leu Ala
        530   535   540

Gln Ala Arg Gly Ala Ala Lys Lys Ala Gly Leu Leu Met Ala Leu Ala
545   550   555   560

Arg Leu Cys Phe Leu Leu Gly Arg Leu Cys Ser Arg Arg Leu Lys Leu
            565   570   575

Ser Gln Ala Arg Val Tyr Phe Glu Glu Ala Leu Gly Ala Leu Glu Gly
            580   585   590

Ser Phe Gly Asp Leu Phe Leu Val Val Ala Val Tyr Ala Asn Leu Ala
        595   600   605

Ser Ile Tyr Arg Lys Gln Lys Asn Arg Glu Lys Cys Ala Gln Val Val
    610   615   620

Pro Lys Ala Met Ala Leu Leu Leu Gly Thr Pro Asp His Ile Cys Ser
625   630   635   640

Thr Glu Ala Glu Gly Glu Leu Leu Gln Leu Ala Leu Arg Arg Ala Val
            645   650   655

Gly Gly Gln Ser Leu Gln Ala Glu Ala Arg Ala Cys Phe Leu Leu Ala
            660   665   670

Arg His His Val His Leu Lys Gln Pro Glu Glu Ala Leu Pro Phe Leu
        675   680   685

Glu Arg Leu Leu Leu Leu His Arg Asp Ser Gly Ala Pro Glu Ala Ala
    690   695   700

Trp Leu Ser Asp Cys Tyr Leu Leu Leu Ala Asp Ile Tyr Ser Arg Lys
705   710   715   720

Cys Leu Pro His Leu Val Leu Ser Cys Val Lys Val Ala Ser Leu Arg
            725   730   735

```
Thr Arg Gly Ser Leu Ala Gly Ser Leu Arg Ser Val Asn Leu Val Leu
        740             745                 750

Gln Asn Ala Pro Gln Pro His Ser Leu Pro Ala Gln Thr Ser His Tyr
        755             760                 765

Leu Arg Gln Ala Leu Ala Ser Leu Thr Pro Gly Thr Gly Gln Ala Leu
    770             775                 780

Arg Gly Pro Leu Tyr Thr Ser Leu Ala Gln Leu Tyr Ser His His Gly
785             790                 795                 800

Cys His Gly Pro Ala Ile Thr Phe Met Thr Gln Ala Val Glu Ala Ser
            805             810                 815

Ala Ile Ala Gly Val Arg Ala Ile Val Asp His Leu Val Ala Leu Ala
        820             825                 830

Trp Leu His Val Leu His Gly Gln Ser Pro Val Ala Leu Asp Ile Leu
        835             840                 845

Gln Ser Val Arg Asp Ala Val Val Ala Ser Glu Asp Gln Glu Gly Val
    850             855                 860

Ile Ala Asn Met Val Ala Val Ala Leu Lys Arg Thr Gly Arg Thr Arg
865             870                 875                 880

Gln Ala Ala Glu Ser Tyr Tyr Arg Ala Leu Arg Val Ala Arg Asp Leu
            885             890                 895

Gly Gln Gln Arg Asn Gln Ala Val Gly Leu Ala Asn Phe Gly Ala Leu
        900             905                 910

Cys Leu His Ala Gly Ala Ser Arg Leu Ala Gln His Tyr Leu Leu Glu
        915             920                 925

Ala Val Arg Leu Phe Ser Arg Leu Pro Leu Gly Glu Cys Gly Arg Asp
    930             935                 940

Phe Thr His Val Leu Leu Gln Leu Gly His Leu Cys Thr Arg Gln Gly
945             950                 955                 960

Pro Ala Gln Gln Gly Lys Gly Tyr Tyr Glu Trp Ala Leu Leu Val Ala
            965             970                 975
```

965

Val Glu Met Gly His Val Glu Ser Gln Leu Arg Ala Val Gln Arg Leu
          980   985   990

Cys His Phe Tyr Ser Ala Val Met Pro Ser Glu Ala Gln Cys Val Ile
          995   1000   1005

Tyr His Glu Leu Gln Leu Ser Pro Ala Cys Lys Val Ala Asp Lys
    1010   1015   1020

Val Leu Glu Gly Gln Leu Leu Glu Thr Ile Ser Gln Leu Tyr Leu
    1025   1030   1035

Ser Leu Gly Thr Glu Arg Ala Tyr Lys Ser Ala Leu Asp Tyr Thr
    1040   1045   1050

Lys Arg Ser Leu Gly Ile Phe Ile Asp Leu Gln Lys Lys Glu Lys
    1055   1060   1065

Glu Ala His Ala Trp Leu Gln Ala Gly Lys Ile Tyr Tyr Ile Leu
    1070   1075   1080

Arg Gln Ser Glu Leu Val Asp Leu Tyr Ile Gln Val Ala Gln Asn
    1085   1090   1095

Val Ala Leu Tyr Thr Gly Asp Pro Asn Leu Gly Leu Glu Leu Phe
    1100   1105   1110

Glu Ala Ala Gly Asp Ile Phe Phe Asp Gly Ala Trp Glu Arg Glu
    1115   1120   1125

Lys Ala Val Ser Phe Tyr Arg Asp Arg Ala Leu Pro Leu Ala Val
    1130   1135   1140

Thr Thr Gly Asn Arg Lys Ala Glu Leu Arg Leu Cys Asn Lys Leu
    1145   1150   1155

Val Ala Leu Leu Ala Thr Leu Glu Glu Pro Gln Glu Gly Leu Glu
    1160   1165   1170

Phe Ala His Met Ala Leu Ala Leu Ser Ile Thr Leu Gly Asp Arg
    1175   1180   1185

Leu Asn Glu Arg Val Ala Tyr His Arg Leu Ala Ala Leu Gln His
    1190   1195   1200

Arg Leu Gly His Gly Glu Leu Ala Glu His Phe Tyr Leu Lys Ala

966

```
        1205                    1210                    1215


Leu Ser  Leu Cys Asn Ser Pro  Leu Glu Phe Asp Glu  Glu Thr Leu
        1220                    1225                    1230


Tyr Tyr  Val Lys Val Tyr Leu  Val Leu Gly Asp Ile  Ile Phe Tyr
        1235                    1240                    1245


Asp Leu  Lys Asp Pro Phe Asp  Ala Ala Gly Tyr Tyr  Gln Leu Ala
        1250                    1255                    1260


Leu Ala  Ala Ala Val Asp Leu  Gly Asn Lys Lys Ala  Gln Leu Lys
        1265                    1270                    1275


Ile Tyr  Thr Arg Leu Ala Thr  Ile Tyr His Asn Phe  Leu Leu Asp
        1280                    1285                    1290


Arg Glu  Lys Ser Leu Phe Phe  Tyr Gln Lys Ala Arg  Thr Phe Ala
        1295                    1300                    1305


Thr Glu  Leu Asn Val Arg Arg  Val Asn Leu Pro Pro  Leu Pro Leu
        1310                    1315                    1320


Cys Gly  Trp Ala Pro Trp Leu  Ala Pro Ser His Pro  Arg
        1325                    1330                    1335
```

<210> 2565
<211> 93
<212> PRT
<213> Homo sapiens

<400> 2565

```
Met Leu Thr Glu Leu Glu Lys Ala Leu Asn Ser Ile Ile Asp Val Tyr
1               5                   10                  15


His Lys Tyr Ser Leu Ile Lys Gly Asn Phe His Ala Val Tyr Arg Asp
            20                  25                  30


Asp Leu Lys Lys Leu Leu Glu Thr Glu Cys Pro Gln Tyr Ile Arg Lys
        35                  40                  45


Lys Gly Ala Asp Val Trp Phe Lys Glu Leu Asp Ile Asn Thr Asp Gly
    50                  55                  60


Ala Val Asn Phe Gln Glu Phe Leu Ile Leu Val Ile Lys Met Gly Val
65                  70                  75                  80
```

```
Ala Ala His Lys Lys Ser His Glu Glu Ser His Lys Glu
                85                      90
```

```
<210>  2566
<211>  1186
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2566
```

```
Met Gly Val Gln Gly Leu Trp Lys Leu Leu Glu Cys Ser Gly Arg Gln
1               5                   10                  15
```

```
Val Ser Pro Glu Ala Leu Glu Gly Lys Ile Leu Ala Val Asp Ile Ser
            20                  25                  30
```

```
Ile Trp Leu Asn Gln Ala Leu Lys Gly Val Arg Asp Arg His Gly Asn
        35                  40                  45
```

```
Ser Ile Glu Asn Pro His Leu Leu Thr Leu Phe His Arg Leu Cys Lys
    50                  55                  60
```

```
Leu Leu Phe Phe Arg Ile Arg Pro Ile Phe Val Phe Asp Gly Asp Ala
65                  70                  75                  80
```

```
Pro Leu Leu Lys Lys Gln Thr Leu Val Lys Arg Arg Gln Arg Lys Asp
                85                  90                  95
```

```
Leu Ala Ser Ser Asp Ser Arg Lys Thr Thr Glu Lys Leu Leu Lys Thr
            100                 105                 110
```

```
Phe Leu Lys Arg Gln Ala Ile Lys Thr Ala Phe Arg Ser Lys Arg Asp
        115                 120                 125
```

```
Glu Ala Leu Pro Ser Leu Thr Gln Val Arg Arg Glu Asn Asp Leu Tyr
    130                 135                 140
```

```
Val Leu Pro Pro Leu Gln Glu Glu Glu Lys His Ser Ser Glu Glu Glu
145                 150                 155                 160
```

```
Asp Glu Lys Glu Trp Gln Glu Arg Met Asn Gln Lys Gln Ala Leu Gln
                165                 170                 175
```

```
Glu Glu Phe Phe His Asn Pro Gln Ala Ile Asp Ile Glu Ser Glu Asp
            180                 185                 190
```

```
Phe Ser Ser Leu Pro Pro Glu Val Lys His Glu Ile Leu Thr Asp Met
```

```
                  195                    200                    205

      Lys Glu Phe Thr Lys Arg Arg Arg Thr Leu Phe Glu Ala Met Pro Glu
          210                215                220


      Glu Ser Asp Asp Phe Ser Gln Tyr Gln Leu Lys Gly Leu Leu Lys Lys
      225                230                235                240


      Asn Tyr Leu Asn Gln His Ile Glu His Val Gln Lys Glu Met Asn Gln
                      245                250                255


      Gln His Ser Gly His Ile Arg Arg Gln Tyr Glu Asp Glu Gly Gly Phe
                  260                265                270


      Leu Lys Glu Val Glu Ser Arg Arg Val Val Ser Glu Asp Thr Ser His
              275                280                285


      Tyr Ile Leu Ile Lys Gly Ile Gln Ala Lys Thr Val Ala Glu Val Asp
          290                295                300


      Ser Glu Ser Leu Pro Ser Ser Ser Lys Met His Gly Met Ser Phe Asp
      305                310                315                320


      Val Lys Ser Ser Pro Cys Glu Lys Leu Lys Thr Glu Lys Glu Pro Asp
                      325                330                335


      Ala Thr Pro Pro Ser Pro Arg Thr Leu Leu Ala Met Gln Ala Ala Leu
                  340                345                350


      Leu Gly Ser Ser Ser Glu Glu Glu Leu Glu Ser Glu Asn Arg Arg Gln
              355                360                365


      Ala Arg Gly Arg Asn Ala Pro Ala Ala Val Asp Glu Gly Ser Ile Ser
          370                375                380


      Pro Arg Thr Leu Ser Ala Ile Lys Arg Ala Leu Asp Asp Asp Glu Asp
      385                390                395                400


      Val Lys Val Cys Ala Gly Asp Asp Val Gln Thr Gly Gly Pro Gly Ala
                      405                410                415


      Glu Glu Met Arg Ile Asn Ser Ser Thr Glu Asn Ser Asp Glu Gly Leu
                  420                425                430


      Lys Val Arg Asp Gly Lys Gly Ile Pro Phe Thr Ala Thr Leu Ala Ser
              435                440                445
```

```
Ser Ser Val Asn Ser Ala Glu Glu His Val Ala Ser Thr Asn Glu Gly
    450             455                 460

Arg Glu Pro Thr Asp Ser Val Pro Lys Glu Gln Met Ser Leu Val His
465             470                 475                 480

Val Gly Thr Glu Ala Phe Pro Ile Ser Asp Glu Ser Met Ile Lys Asp
            485             490                 495

Arg Lys Asp Arg Leu Pro Leu Glu Ser Ala Val Val Arg His Ser Asp
            500             505                 510

Ala Pro Gly Leu Pro Asn Gly Arg Glu Leu Thr Pro Ala Ser Pro Thr
        515             520                 525

Cys Thr Asn Ser Val Ser Lys Asn Glu Thr His Ala Glu Val Leu Glu
    530             535                 540

Gln Gln Asn Glu Leu Cys Pro Tyr Glu Ser Lys Phe Asp Ser Ser Leu
545             550             555                 560

Leu Ser Ser Asp Asp Glu Thr Lys Cys Lys Pro Asn Ser Ala Ser Glu
            565             570                 575

Val Ile Gly Pro Val Ser Leu Gln Glu Thr Ser Ser Ile Val Ser Val
        580             585                 590

Pro Ser Glu Ala Val Asp Asn Val Glu Asn Val Val Ser Phe Asn Ala
    595             600                 605

Lys Glu His Glu Asn Phe Leu Glu Thr Ile Gln Glu Gln Gln Thr Thr
    610             615                 620

Glu Ser Ala Gly Gln Asp Leu Ile Ser Ile Pro Lys Ala Val Glu Pro
625             630                 635                 640

Met Glu Ile Asp Ser Glu Glu Ser Glu Ser Asp Gly Ser Phe Ile Glu
            645             650                 655

Val Gln Ser Val Ile Ser Asp Glu Glu Leu Gln Ala Glu Phe Pro Glu
        660             665                 670

Thr Ser Lys Pro Pro Ser Glu Gln Gly Glu Glu Glu Leu Val Gly Thr
    675             680                 685
```

```
Arg Glu Gly Glu Ala Pro Ala Glu Ser Glu Ser Leu Leu Arg Asp Asn
    690             695             700

Ser Glu Arg Asp Asp Val Asp Gly Glu Pro Gln Glu Ala Glu Lys Asp
705             710             715             720

Ala Glu Asp Ser Leu His Glu Trp Gln Asp Ile Asn Leu Glu Glu Leu
            725             730             735

Glu Thr Leu Glu Ser Asn Leu Leu Ala Gln Gln Asn Ser Leu Lys Ala
            740             745             750

Gln Lys Gln Gln Gln Glu Arg Ile Ala Ala Thr Val Thr Gly Gln Met
        755             760             765

Phe Leu Glu Ser Gln Glu Leu Leu Arg Leu Phe Gly Ile Pro Tyr Ile
    770             775             780

Gln Ala Pro Met Glu Ala Glu Ala Gln Cys Ala Ile Leu Asp Leu Thr
785             790             795             800

Asp Gln Thr Ser Gly Thr Ile Thr Asp Asp Ser Asp Ile Trp Leu Phe
            805             810             815

Gly Ala Arg His Val Tyr Arg Asn Phe Phe Asn Lys Asn Lys Phe Val
            820             825             830

Glu Tyr Tyr Gln Tyr Val Asp Phe His Asn Gln Leu Gly Leu Asp Arg
        835             840             845

Asn Lys Leu Ile Asn Leu Ala Tyr Leu Leu Gly Ser Asp Tyr Thr Glu
    850             855             860

Gly Ile Pro Thr Val Gly Cys Val Thr Ala Met Glu Ile Leu Asn Glu
865             870             875             880

Phe Pro Gly His Gly Leu Glu Pro Leu Leu Lys Phe Ser Glu Trp Trp
            885             890             895

His Glu Ala Gln Lys Asn Pro Lys Ile Arg Pro Asn Pro His Asp Thr
        900             905             910

Lys Val Lys Lys Lys Leu Arg Thr Leu Gln Leu Thr Pro Gly Phe Pro
    915             920             925
```

```
Asn Pro Ala Val Ala Glu Ala Tyr Leu Lys Pro Val Val Asp Asp Ser
    930             935             940

Lys Gly Ser Phe Leu Trp Gly Lys Pro Asp Leu Asp Lys Ile Arg Glu
945             950             955             960

Phe Cys Gln Arg Tyr Phe Gly Trp Asn Arg Thr Lys Thr Asp Glu Ser
            965             970             975

Leu Phe Pro Val Leu Lys Gln Leu Asp Ala Gln Gln Thr Gln Leu Arg
        980             985             990

Ile Asp Ser Phe Phe Arg Leu Ala Gln Gln Glu Lys Glu Asp Ala Lys
    995             1000            1005

Arg Ile Lys Ser Gln Arg Leu Asn Arg Ala Val Thr Cys Met Leu
    1010            1015            1020

Arg Lys Glu Lys Glu Ala Ala Ala Ser Glu Ile Glu Ala Val Ser
    1025            1030            1035

Val Ala Met Glu Lys Glu Phe Glu Leu Leu Asp Lys Ala Lys Arg
    1040            1045            1050

Lys Thr Gln Lys Arg Gly Ile Thr Asn Thr Leu Glu Glu Ser Ser
    1055            1060            1065

Ser Leu Lys Arg Lys Arg Leu Ser Asp Ser Lys Arg Lys Asn Thr
    1070            1075            1080

Cys Gly Gly Phe Leu Gly Glu Thr Cys Leu Ser Glu Ser Ser Asp
    1085            1090            1095

Gly Ser Ser Ser Glu His Ala Glu Ser Ser Ser Leu Met Asn Val
    1100            1105            1110

Gln Arg Arg Thr Ala Ala Lys Glu Pro Lys Thr Ser Ala Ser Asp
    1115            1120            1125

Ser Gln Asn Ser Val Lys Glu Ala Pro Val Lys Asn Gly Gly Ala
    1130            1135            1140

Thr Thr Ser Ser Ser Ser Asp Ser Asp Asp Asp Gly Gly Lys Glu
    1145            1150            1155

Lys Met Val Leu Val Thr Ala Arg Ser Val Phe Gly Lys Lys Arg
```

972

1160   1165   1170

Arg Lys Leu Arg Arg Ala Arg Gly Arg Lys Arg Lys Thr
    1175   1180   1185

<210> 2567
<211> 84
<212> PRT
<213> Homo sapiens

<400> 2567

Met Pro Leu Ala Lys Asp Leu Leu His Pro Ser Pro Glu Glu Glu Lys
1   5   10   15

Arg Lys His Lys Lys Lys Arg Leu Val Gln Ser Pro Asn Ser Tyr Phe
        20   25   30

Met Asp Val Lys Cys Pro Gly Cys Tyr Lys Ile Thr Thr Val Phe Ser
        35   40   45

His Ala Gln Thr Val Val Leu Cys Val Gly Cys Ser Thr Val Leu Cys
        50   55   60

Gln Pro Thr Gly Gly Lys Ala Arg Leu Thr Glu Gly Cys Ser Phe Arg
65   70   75   80

Arg Lys Gln His

<210> 2568
<211> 691
<212> PRT
<213> Homo sapiens

<400> 2568

Met Asp Gly Cys Lys Lys Glu Leu Pro Arg Leu Gln Glu Pro Glu Glu
1   5   10   15

Asp Glu Asp Cys Tyr Ile Leu Asn Val Gln Ser Ser Ser Asp Asp Thr
            20   25   30

Ser Gly Ser Ser Val Ala Arg Arg Ala Pro Lys Arg Gln Ala Ser Cys
        35   40   45

Ile Leu Asn Val Gln Ser Arg Ser Gly Asp Thr Ser Gly Ser Ser Val
    50   55   60

```
Ala Arg Arg Ala Pro Lys Arg Gln Ala Ser Ser Val Val Val Ile Asp
65            70          75              80


Ser Asp Ser Asp Glu Glu Cys His Thr His Glu Glu Lys Lys Ala Lys
            85          90              95


Leu Leu Glu Ile Asn Ser Asp Asp Glu Ser Pro Glu Cys Cys His Val
            100         105             110


Lys Pro Ala Ile Gln Glu Pro Pro Ile Val Ile Ser Asp Asp Asp Asn
        115         120             125


Asp Asp Asp Asn Gly Asn Asp Leu Glu Val Pro Asp Asp Asn Ser Asp
    130             135             140


Asp Ser Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser Glu Ala Pro Asp
145             150             155             160


Asp Asn Ser Asp Asp Ser Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser
            165             170             175


Glu Ala Pro Asp Asp Asn Ser Asp Asp Ser Asp Val Pro Asp Asp Asn
        180             185             190


Ser Asp Asp Ser Ser Asp Asp Asn Ser Asp Asp Ser Ser Asp Asp Asn
    195             200             205


Ser Asp Asp Ser Asp Val Pro Asp Asp Lys Ser Asp Asp Ser Asp Val
    210             215             220


Pro Asp Asp Ser Ser Asp Asp Ser Asp Val Pro Asp Asp Ser Ser Asp
225             230             235             240


Asp Ser Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser Glu Ala Pro Asp
            245             250             255


Asp Ser Ser Asp Asp Ser Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser
        260             265             270


Glu Ala Pro Asp Asp Ser Ser Asp Asp Ser Glu Ala Ser Asp Asp Ser
    275             280             285


Ser Asp Asp Ser Glu Ala Ser Asp Asp Ser Ser Asp Asp Ser Glu Ala
    290             295             300


Pro Asp Asp Lys Ser Asp Asp Ser Asp Val Pro Glu Asp Lys Ser Asp
```

                    305   310   315   320

Asp Ser Asp Val Pro Asp Asp Asn Ser Asp Asp Leu Glu Val Pro Val
                325   330   335

Pro Ala Glu Asp Leu Cys Asn Glu Gly Gln Ile Ala Ser Asp Glu Glu
            340   345   350

Glu Leu Val Glu Ala Ala Ala Ala Val Ser Gln His Asp Ser Ser Asp
        355   360   365

Asp Ala Gly Glu Gln Asp Leu Gly Glu Asn Leu Ser Lys Pro Pro Ser
    370   375   380

Asp Pro Glu Ala Asn Pro Glu Val Ser Glu Arg Lys Leu Pro Thr Glu
385   390   395   400

Glu Glu Pro Ala Pro Val Val Glu Gln Ser Gly Lys Arg Lys Ser Lys
                405   410   415

Thr Lys Thr Ile Val Glu Pro Pro Lys Arg Gln Thr Lys Thr Lys
                420   425   430

Asn Ile Val Glu Pro Pro Arg Lys Arg Gln Thr Lys Thr Lys Asn Ile
        435   440   445

Val Glu Pro Leu Arg Lys Arg Lys Ala Lys Thr Lys Asn Val Ser Val
    450   455   460

Thr Pro Gly His Lys Lys Arg Gly Pro Ser Lys Lys Lys Pro Gly Ala
465   470   475   480

Ala Lys Val Glu Lys Arg Lys Thr Arg Thr Pro Lys Cys Lys Val Pro
                485   490   495

Gly Cys Phe Leu Gln Asp Leu Glu Lys Ser Lys Lys Tyr Ser Gly Lys
                500   505   510

Asn Leu Lys Arg Asn Lys Asp Glu Leu Val Gln Arg Ile Tyr Asp Leu
        515   520   525

Phe Asn Arg Ser Val Cys Asp Lys Lys Leu Pro Glu Lys Leu Arg Ile
        530   535   540

Gly Trp Asn Asn Lys Met Val Lys Thr Ala Gly Leu Cys Ser Thr Gly
545   550   555   560

                              975

```
Glu Met Trp Tyr Pro Lys Trp Arg Arg Phe Ala Lys Ile Gln Ile Gly
              565             570             575

Leu Lys Val Cys Asp Ser Ala Asp Arg Ile Arg Asp Thr Leu Ile His
              580             585             590

Glu Met Cys His Ala Ala Ser Trp Leu Ile Asp Gly Ile His Asp Ser
          595             600             605

His Gly Asp Ala Trp Lys Tyr Tyr Ala Arg Lys Ser Asn Arg Ile His
      610             615             620

Pro Glu Leu Pro Arg Val Thr Arg Cys His Asn Tyr Lys Ile Asn Tyr
625             630             635             640

Lys Val His Tyr Glu Cys Thr Gly Cys Lys Thr Arg Ile Gly Cys Tyr
              645             650             655

Thr Lys Ser Leu Asp Thr Ser Arg Phe Ile Cys Ala Lys Cys Lys Gly
              660             665             670

Ser Leu Val Met Val Pro Leu Thr Gln Lys Asp Gly Thr Arg Ile Val
          675             680             685

Pro His Val
      690


<210> 2569
<211> 101
<212> PRT
<213> Homo sapiens

<400> 2569

Met Ser Asp Gln Glu Ala Lys Pro Ser Thr Glu Asp Leu Gly Asp Lys
1               5               10              15

Lys Glu Gly Glu Tyr Ile Lys Leu Lys Val Ile Gly Gln Asp Ser Ser
              20              25              30

Glu Ile His Phe Lys Val Lys Met Thr Thr His Leu Lys Lys Leu Lys
          35              40              45

Glu Ser Tyr Cys Gln Arg Gln Gly Val Pro Met Asn Ser Leu Arg Phe
      50              55              60
```

```
Leu Phe Glu Gly Gln Arg Ile Ala Asp Asn His Thr Pro Lys Glu Leu
65                  70              75                  80


Gly Met Glu Glu Glu Asp Val Ile Glu Val Tyr Gln Glu Gln Thr Gly
                85                  90                  95


Gly His Ser Thr Val
            100
```


<210>   2570
<211>   93
<212>   PRT
<213>   Homo sapiens

<400>   2570

```
Met Ser Gly Leu Arg Val Tyr Ser Thr Ser Val Thr Gly Ser Arg Glu
1               5                   10                  15


Ile Lys Ser Gln Gln Ser Glu Val Thr Arg Ile Leu Asp Gly Lys Arg
                20                  25                  30


Ile Gln Tyr Gln Leu Val Asp Ile Ser Gln Asp Asn Ala Leu Arg Asp
            35                  40                  45


Glu Met Arg Ala Leu Ala Gly Asn Pro Lys Ala Thr Pro Pro Gln Ile
    50                  55                  60


Val Asn Gly Asp Gln Tyr Cys Gly Asp Tyr Glu Leu Phe Val Glu Ala
65                  70                  75                  80


Val Glu Gln Asn Thr Leu Gln Glu Phe Leu Lys Leu Ala
                85                  90
```


<210>   2571
<211>   666
<212>   PRT
<213>   Homo sapiens

<400>   2571

```
Met Thr Pro Pro Pro Gly Arg Ala Ala Pro Ser Ala Pro Arg Ala
1               5                   10                  15


Arg Val Pro Gly Pro Pro Ala Arg Leu Gly Leu Pro Leu Arg Leu Arg
            20                  25                  30


Leu Leu Leu Leu Leu Trp Ala Ala Ala Ala Ser Ala Gln Gly His Leu
        35                  40                  45
```


977

```
Arg Ser Gly Pro Arg Ile Phe Ala Val Trp Lys Gly His Val Gly Gln
    50              55              60


Asp Arg Val Asp Phe Gly Gln Thr Glu Pro His Thr Val Leu Phe His
65              70              75              80


Glu Pro Gly Ser Ser Ser Val Trp Val Gly Gly Arg Gly Lys Val Tyr
            85              90              95


Leu Phe Asp Phe Pro Glu Gly Lys Asn Ala Ser Val Arg Thr Val Asn
            100             105             110


Ile Gly Ser Thr Lys Gly Ser Cys Leu Asp Lys Arg Asp Cys Glu Asn
        115             120             125


Tyr Ile Thr Leu Leu Glu Arg Arg Ser Glu Gly Leu Leu Ala Cys Gly
    130             135             140


Thr Asn Ala Arg His Pro Ser Cys Trp Asn Leu Val Asn Gly Thr Val
145             150             155             160


Val Pro Leu Gly Glu Met Arg Gly Tyr Ala Pro Phe Ser Pro Asp Glu
 -              165             170             175


Asn Ser Leu Val Leu Phe Glu Gly Asp Glu Val Tyr Ser Thr Ile Arg
            180             185             190


Lys Gln Glu Tyr Asn Gly Lys Ile Pro Arg Phe Arg Arg Ile Arg Gly
    195             200             205


Glu Ser Glu Leu Tyr Thr Ser Asp Thr Val Met Gln Asn Pro Gln Phe
    210             215             220


Ile Lys Ala Thr Ile Val His Gln Asp Gln Ala Tyr Asp Asp Lys Ile
225             230             235             240


Tyr Tyr Phe Phe Arg Glu Asp Asn Pro Asp Lys Asn Pro Glu Ala Pro
            245             250             255


Leu Asn Val Ser Arg Val Ala Gln Leu Cys Arg Gly Asp Gln Gly Gly
            260             265             270


Glu Ser Ser Leu Ser Val Ser Lys Trp Asn Thr Phe Leu Lys Ala Met
            275             280             285
```

978

```
Leu Val Cys Ser Asp Ala Ala Thr Asn Lys Asn Phe Asn Arg Leu Gln
    290             295             300

Asp Val Phe Leu Leu Pro Asp Pro Ser Gly Gln Trp Arg Asp Thr Arg
305             310             315             320

Val Tyr Gly Val Phe Ser Asn Pro Trp Asn Tyr Ser Ala Val Cys Val
            325             330             335

Tyr Ser Leu Gly Asp Ile Asp Lys Val Phe Arg Thr Ser Ser Leu Lys
        340             345             350

Gly Tyr His Ser Ser Leu Pro Asn Pro Arg Pro Gly Lys Cys Leu Pro
        355             360             365

Asp Gln Gln Pro Ile Pro Thr Glu Thr Phe Gln Val Ala Asp Arg His
    370             375             380

Pro Glu Val Ala Gln Arg Val Glu Pro Met Gly Pro Leu Lys Thr Pro
385             390             395             400

Leu Phe His Ser Lys Tyr His Tyr Gln Lys Val Ala Val His Arg Met
            405             410             415

Gln Ala Ser His Gly Glu Thr Phe His Val Leu Tyr Leu Thr Thr Asp
        420             425             430

Arg Gly Thr Ile His Lys Val Val Glu Pro Gly Glu Gln Glu His Ser
        435             440             445

Phe Ala Phe Asn Ile Met Glu Ile Gln Pro Phe Arg Arg Ala Ala Ala
    450             455             460

Ile Gln Thr Met Ser Leu Asp Ala Glu Arg Arg Lys Leu Tyr Val Ser
465             470             475             480

Ser Gln Trp Glu Val Ser Gln Val Pro Leu Asp Leu Cys Glu Val Tyr
            485             490             495

Gly Gly Gly Cys His Gly Cys Leu Met Ser Arg Asp Pro Tyr Cys Gly
        500             505             510

Trp Asp Gln Gly Arg Cys Ile Ser Ile Tyr Ser Ser Glu Arg Ser Val
    515             520             525

Leu Gln Ser Ile Asn Pro Ala Glu Pro His Lys Glu Cys Pro Asn Pro
```

530   535   540

Lys Pro Asp Lys Ala Pro Leu Gln Lys Val Ser Leu Ala Pro Asn Ser
545   550   555   560

Arg Tyr Tyr Leu Ser Cys Pro Met Glu Ser Arg His Ala Thr Tyr Ser
               565   570   575

Trp Arg His Lys Glu Asn Val Glu Gln Ser Cys Glu Pro Gly His Gln
            580   585   590

Ser Pro Asn Cys Ile Leu Phe Ile Glu Asn Leu Thr Ala Gln Gln Tyr
         595   600   605

Gly His Tyr Phe Cys Glu Ala Gln Glu Gly Ser Tyr Phe Arg Glu Ala
      610   615   620

Gln His Trp Gln Leu Leu Pro Glu Asp Gly Ile Met Ala Glu His Leu
625   630   635   640

Leu Gly His Ala Cys Ala Leu Ala Ala Ser Leu Trp Leu Gly Val Leu
            645   650   655

Pro Thr Leu Thr Leu Gly Leu Leu Val His
            660   665

<210> 2572
<211> 162
<212> PRT
<213> Homo sapiens

<400> 2572

Met Arg Ser Ser Pro Gly Asn Met Glu Arg Ile Val Ile Cys Leu Met
1   5   10   15

Val Ile Phe Leu Gly Thr Leu Val His Lys Ser Ser Ser Gln Gly Gln
            20   25   30

Asp Arg His Met Ile Arg Met Arg Gln Leu Ile Asp Ile Val Asp Gln
         35   40   45

Leu Lys Asn Tyr Val Asn Asp Leu Val Pro Glu Phe Leu Pro Ala Pro
      50   55   60

Glu Asp Val Glu Thr Asn Cys Glu Trp Ser Ala Phe Ser Cys Phe Gln
65   70   75   80

980

```
Lys Ala Gln Leu Lys Ser Ala Asn Thr Gly Asn Asn Glu Arg Ile Ile
                85                  90                  95

Asn Val Ser Ile Lys Lys Leu Lys Arg Lys Pro Pro Ser Thr Asn Ala
                100             105                 110

Gly Arg Arg Gln Lys His Arg Leu Thr Cys Pro Ser Cys Asp Ser Tyr
            115                 120                 125

Glu Lys Lys Pro Pro Lys Glu Phe Leu Glu Arg Phe Lys Ser Leu Leu
        130                 135                 140

Gln Lys Met Ile His Gln His Leu Ser Ser Arg Thr His Gly Ser Glu
145                 150                 155                 160

Asp Ser
```

```
<210>  2573
<211>  1050
<212>  PRT
<213>  Homo sapiens

<400>  2573
```

```
Met Leu Cys Trp Gly Tyr Trp Ser Leu Gly Gln Pro Gly Ile Ser Thr
1               5                   10                  15

Asn Leu Gln Gly Ile Val Ala Glu Pro Gln Val Cys Gly Phe Ile Ser
                20                  25                  30

Asp Arg Ser Val Lys Glu Val Ala Cys Gly Gly Asn His Ser Val Phe
            35                  40                  45

Leu Leu Glu Asp Gly Glu Val Tyr Thr Cys Gly Leu Asn Thr Lys Gly
        50                  55                  60

Gln Leu Gly His Glu Arg Glu Gly Asn Lys Pro Glu Gln Ile Gly Ala
65                  70                  75                  80

Leu Ala Asp Gln His Ile Ile His Val Ala Cys Gly Glu Ser His Ser
                85                  90                  95

Leu Ala Leu Ser Asp Arg Gly Gln Leu Phe Ser Trp Gly Ala Gly Ser
                100                 105                 110

Asp Gly Gln Leu Gly Leu Met Thr Thr Glu Asp Ser Val Ala Val Pro
```

      115   120   125

Arg Leu Ile Gln Lys Leu Asn Gln Gln Thr Ile Leu Gln Val Ser Cys
   130   135   140

Gly Asn Trp His Cys Leu Ala Leu Ala Ala Asp Gly Gln Phe Phe Thr
145   150   155   160

Trp Gly Lys Asn Ser His Gly Gln Leu Gly Leu Gly Lys Glu Phe Pro
      165   170   175

Ser Gln Ala Ser Pro Gln Arg Val Arg Ser Leu Glu Gly Ile Pro Leu
     180   185   190

Ala Gln Val Ala Ala Gly Gly Ala His Ser Phe Ala Leu Ser Leu Ser
    195   200   205

Gly Ala Val Phe Gly Trp Gly Met Asn Asn Ala Gly Gln Leu Gly Leu
   210   215   220

Ser Asp Glu Lys Asp Arg Glu Ser Pro Cys His Val Lys Leu Leu Arg
225   230   235   240

Thr Gln Lys Val Val Tyr Ile Ser Cys Gly Glu Glu His Thr Ala Val
    245   250   255

Leu Thr Lys Ser Gly Gly Val Phe Thr Phe Gly Ala Gly Ser Cys Gly
    260   265   270

Gln Leu Gly His Asp Ser Met Asn Asp Glu Val Asn Pro Arg Arg Val
    275   280   285

Leu Glu Leu Met Gly Ser Glu Val Thr Gln Ile Ala Cys Gly Arg Gln
   290   295   300

His Thr Leu Ala Phe Val Pro Ser Ser Gly Leu Ile Tyr Ala Phe Gly
305   310   315   320

Cys Gly Ala Arg Gly Gln Leu Gly Thr Gly His Thr Cys Asn Val Lys
    325   330   335

Cys Pro Ser Pro Val Lys Gly Tyr Trp Ala Ala His Ser Gly Gln Leu
    340   345   350

Ser Ala Arg Ala Asp Arg Phe Lys Tyr His Ile Val Lys Gln Ile Phe
   355   360   365

```
Ser Gly Gly Asp Gln Thr Phe Val Leu Cys Ser Lys Tyr Glu Asn Tyr
    370             375             380

Ser Pro Ala Val Asp Phe Arg Thr Met Asn Gln Ala His Tyr Thr Ser
385             390             395                         400

Leu Ile Asn Asp Glu Thr Ile Ala Val Trp Arg Gln Lys Leu Ser Glu
            405             410             415

His Asn Asn Ala Asn Thr Ile Asn Gly Val Val Gln Ile Leu Ser Ser
            420             425             430

Ala Ala Cys Trp Asn Gly Ser Phe Leu Glu Lys Lys Ile Asp Glu His
        435             440             445

Phe Lys Thr Ser Pro Lys Ile Pro Gly Ile Asp Leu Asn Ser Thr Arg
    450             455             460

Val Leu Phe Glu Lys Leu Met Asn Ser Gln His Ser Met Ile Leu Glu
465             470             475             480

Gln Ile Leu Asn Ser Phe Glu Ser Cys Leu Ile Pro Gln Leu Ser Ser
            485             490             495

Ser Pro Pro Asp Val Glu Ala Met Arg Ile Tyr Leu Ile Leu Pro Glu
        500             505             510

Phe Pro Leu Leu Gln Asp Ser Lys Tyr Tyr Ile Thr Leu Thr Ile Pro
    515             520             525

Leu Ala Met Ala Ile Leu Arg Leu Asp Thr Asn Pro Ser Lys Val Leu
    530             535             540

Asp Asn Trp Trp Ser Gln Val Cys Pro Lys Tyr Phe Met Lys Leu Val
545             550             555             560

Asn Leu Tyr Lys Gly Ala Val Leu Tyr Leu Leu Arg Gly Arg Lys Thr
            565             570             575

Phe Leu Ile Pro Val Leu Phe Asn Asn Tyr Ile Thr Ala Ala Leu Lys
        580             585             590

Leu Leu Glu Lys Leu Tyr Lys Val Asn Leu Lys Val Lys His Val Glu
    595             600             605
```

```
Tyr Asp Thr Phe Tyr Ile Pro Glu Ile Ser Asn Leu Val Asp Ile Gln
    610             615         620

Glu Asp Tyr Leu Met Trp Phe Leu His Gln Ala Gly Met Lys Ala Arg
625             630         635                 640

Pro Ser Ile Ile Gln Asp Thr Val Thr Leu Cys Ser Tyr Pro Phe Ile
            645             650             655

Phe Asp Ala Gln Ala Lys Thr Lys Met Leu Gln Thr Asp Ala Glu Leu
        660             665             670

Gln Met Gln Val Ala Val Asn Gly Ala Asn Leu Gln Asn Val Phe Met
        675             680             685

Leu Leu Thr Leu Glu Pro Leu Leu Ala Arg Ser Pro Phe Leu Val Leu
        690             695         700

His Val Arg Arg Asn Asn Leu Val Gly Asp Ala Leu Arg Glu Leu Ser
705             710             715                 720

Ile His Ser Asp Ile Asp Leu Lys Lys Pro Leu Lys Val Ile Phe Asp
            725             730             735

Gly Glu Glu Ala Val Asp Ala Gly Gly Val Thr Lys Glu Phe Phe Leu
        740             745             750

Leu Leu Leu Lys Glu Leu Leu Asn Pro Ile Tyr Gly Met Phe Thr Tyr
        755             760         765

Tyr Gln Asp Ser Asn Leu Leu Trp Phe Ser Asp Thr Cys Phe Val Glu
    770             775         780

His Asn Trp Phe His Leu Ile Gly Ile Thr Cys Gly Leu Ala Ile Tyr
785             790             795                 800

Asn Ser Thr Val Val Asp Leu His Phe Pro Leu Ala Leu Tyr Lys Lys
            805             810             815

Leu Leu Asn Val Lys Pro Gly Leu Glu Asp Leu Lys Glu Leu Ser Pro
        820             825             830

Thr Glu Gly Arg Ser Leu Gln Glu Leu Leu Asp Tyr Pro Gly Glu Asp
        835             840         845
```

```
Val Glu Glu Thr Phe Cys Leu Asn Phe Thr Ile Cys Arg Glu Ser Tyr
850                 855                 860


Gly Val Ile Glu Gln Lys Lys Leu Ile Pro Gly Gly Asp Asn Val Thr
865                 870                 875                 880


Val Cys Lys Asp Asn Arg Gln Glu Phe Val Asp Ala Tyr Val Asn Tyr
                885                 890                 895


Val Phe Gln Ile Ser Val His Glu Trp Tyr Thr Ala Phe Ser Ser Gly
                900                 905                 910


Phe Leu Lys Val Cys Gly Gly Lys Val Leu Glu Leu Phe Gln Pro Ser
        915                 920                 925


Glu Leu Arg Ala Met Met Val Gly Asn Ser Asn Tyr Asn Trp Glu Glu
    930                 935                 940


Leu Glu Glu Thr Ala Ile Tyr Lys Gly Asp Tyr Ser Ala Thr His Pro
945                 950                 955                 960


Thr Val Lys Leu Phe Trp Glu Thr Phe His Glu Phe Pro Leu Glu Lys
                965                 970                 975


Lys Lys Lys Phe Leu Leu Phe Leu Thr Gly Ser Asp Arg Ile Pro Ile
                980                 985                 990


Tyr Gly Met Ala Ser Leu Gln Ile Val Ile Gln Ser Thr Ala Ser Gly
        995                 1000                1005


Glu Glu Tyr Leu Pro Val Ala His Thr Cys Tyr Asn Leu Leu Asp
    1010                1015                1020


Leu Pro Lys Tyr Ser Ser Lys Glu Ile Leu Ser Ala Arg Leu Thr
    1025                1030                1035


Gln Ala Leu Asp Asn Tyr Glu Gly Phe Ser Leu Ala
    1040                1045                1050


<210> 2574
<211> 369
<212> PRT
<213> Homo sapiens

<400> 2574

Met Arg Ala Cys Ile Ser Leu Val Leu Ala Val Leu Cys Gly Leu Ala
1               5                   10                  15
```

Trp Ala Glu Asp His Lys Glu Ser Glu Pro Leu Pro Gln Leu Glu Glu
        20   25   30

Glu Thr Glu Glu Ala Leu Ala Ser Asn Leu Tyr Ser Ala Pro Thr Ser
        35   40   45

Cys Gln Gly Arg Cys Tyr Glu Ala Phe Asp Lys His His Gln Cys His
        50   55   60

Cys Asn Ala Arg Cys Gln Glu Phe Gly Asn Cys Cys Lys Asp Phe Glu
65   70   75   80

Ser Leu Cys Ser Asp His Glu Val Ser His Ser Ser Asp Ala Ile Thr
                85   90   95

Lys Glu Glu Ile Gln Ser Ile Ser Glu Lys Ile Tyr Arg Ala Asp Thr
            100   105   110

Asn Lys Ala Gln Lys Glu Asp Ile Val Leu Asn Ser Gln Asn Cys Ile
        115   120   125

Ser Pro Ser Glu Thr Arg Asn Gln Val Asp Arg Cys Pro Lys Pro Leu
        130   135   140

Phe Thr Tyr Val Asn Glu Lys Leu Phe Ser Lys Pro Thr Tyr Ala Ala
145   150   155   160

Phe Ile Asn Leu Leu Asn Asn Tyr Gln Arg Ala Thr Gly His Gly Glu
                165   170   175

His Phe Ser Ala Gln Glu Leu Ala Glu Gln Asp Ala Phe Leu Arg Glu
            180   185   190

Ile Met Lys Thr Ala Val Met Lys Glu Leu Tyr Ser Phe Leu His His
        195   200   205

Gln Asn Arg Tyr Gly Ser Glu Gln Glu Phe Val Asp Asp Leu Lys Asn
        210   215   220

Met Trp Phe Gly Leu Tyr Ser Arg Gly Asn Glu Glu Gly Asp Ser Ser
225   230   235   240

Gly Phe Glu His Val Phe Ser Gly Glu Val Lys Lys Gly Lys Val Thr
                245   250   255

986

```
Gly Phe His Asn Trp Ile Arg Phe Tyr Leu Glu Glu Lys Glu Gly Leu
            260             265             270

Val Asp Tyr Tyr Ser His Ile Tyr Asp Gly Pro Trp Asp Ser Tyr Pro
        275             280             285

Asp Val Leu Ala Met Gln Phe Asn Trp Asp Gly Tyr Tyr Lys Glu Val
        290             295             300

Gly Ser Ala Phe Ile Gly Ser Ser Pro Glu Phe Glu Phe Ala Leu Tyr
305             310             315             320

Ser Leu Cys Phe Ile Ala Arg Pro Gly Lys Val Cys Gln Leu Ser Leu
            325             330             335

Gly Gly Tyr Pro Leu Ala Val Arg Thr Tyr Thr Trp Asp Lys Ser Thr
            340             345             350

Tyr Gly Asn Gly Lys Lys Tyr Ile Ala Thr Ala Tyr Ile Val Ser Ser
            355             360             365

Thr
```

```
<210>  2575
<211>  90
<212>  PRT
<213>  Homo sapiens

<400>  2575
```

```
Met Asp Pro Leu Arg Ala Gln Gln Leu Ala Ala Glu Leu Glu Val Glu
1               5               10              15

Met Met Ala Asp Met Tyr Asn Arg Met Thr Ser Ala Cys His Arg Lys
            20              25              30

Cys Val Pro Pro His Tyr Lys Glu Ala Glu Leu Ser Lys Gly Glu Ser
        35              40              45

Val Cys Leu Asp Arg Cys Val Ser Lys Tyr Leu Asp Ile His Glu Arg
        50              55              60

Met Gly Lys Lys Leu Thr Glu Leu Ser Met Gln Asp Glu Glu Leu Met
65              70              75              80

Lys Arg Val Gln Gln Ser Ser Gly Pro Ala
```

                        85   .   90

<210> 2576
<211> 426
<212> PRT
<213> Homo sapiens

<400> 2576

Met Ala Asn Asp Ser Gly Gly Pro Gly Gly Pro Ser Pro Ser Glu Arg
1   5   10   15

Asp Arg Gln Tyr Cys Glu Leu Cys Gly Lys Met Glu Asn Leu Leu Arg
            20   25   30

Cys Ser Arg Cys Arg Ser Ser Phe Tyr Cys Cys Lys Glu His Gln Arg
        35   40   45

Gln Asp Trp Lys Lys His Lys Leu Val Cys Gln Gly Ser Glu Gly Ala
    50   55   60

Leu Gly His Gly Val Gly Pro His Gln His Ser Gly Pro Ala Pro Pro
65   70   75   80

Ala Ala Val Pro Pro Pro Arg Ala Gly Ala Arg Glu Pro Arg Lys Ala
            85   90   95

Ala Ala Arg Arg Asp Asn Ala Ser Gly Asp Ala Ala Lys Gly Lys Val
            100   105   110

Lys Ala Lys Pro Pro Ala Asp Pro Ala Ala Ala Ala Ser Pro Cys Arg
        115   120   125

Ala Ala Ala Gly Gly Gln Gly Ser Ala Val Ala Ala Glu Ala Glu Pro
    130   135   140

Gly Lys Glu Glu Pro Pro Ala Arg Ser Ser Leu Phe Gln Glu Lys Ala
145   150   155   160

Asn Leu Tyr Pro Pro Ser Asn Thr Pro Gly Asp Ala Leu Ser Pro Gly
            165   170   175

Gly Gly Leu Arg Pro Asn Gly Gln Thr Lys Pro Leu Pro Ala Leu Lys
            180   185   190

Leu Ala Leu Glu Tyr Ile Val Pro Cys Met Asn Lys His Gly Ile Cys
        195   200   205

Val Val Asp Asp Phe Leu Gly Lys Glu Thr Gly Gln Gln Ile Gly Asp
    210   215   220

Glu Val Arg Ala Leu His Asp Thr Gly Lys Phe Thr Asp Gly Gln Leu
225   230   235   240

Val Ser Gln Lys Ser Asp Ser Ser Lys Asp Ile Arg Gly Asp Lys Ile
            245   250   255

Thr Trp Ile Glu Gly Lys Glu Pro Gly Cys Glu Thr Ile Gly Leu Leu
        260   265   270

Met Ser Ser Met Asp Asp Leu Ile Arg His Cys Asn Gly Lys Leu Gly
        275   280   285

Ser Tyr Lys Ile Asn Gly Arg Thr Lys Ala Met Val Ala Cys Tyr Pro
    290   295   300

Gly Asn Gly Thr Gly Tyr Val Arg His Val Asp Asn Pro Asn Gly Asp
305   310   315   320

Gly Arg Cys Val Thr Cys Ile Tyr Tyr Leu Asn Lys Asp Trp Asp Ala
            325   330   335

Lys Val Ser Gly Gly Ile Leu Arg Ile Phe Pro Glu Gly Lys Ala Gln
        340   345   350

Phe Ala Asp Ile Glu Pro Lys Phe Asp Arg Leu Leu Phe Phe Trp Ser
    355   360   365

Asp Arg Arg Asn Pro His Glu Val Gln Pro Ala Tyr Ala Thr Arg Tyr
    370   375   380

Ala Ile Thr Val Trp Tyr Phe Asp Ala Asp Glu Arg Ala Arg Ala Lys
385   390   395   400

Val Lys Tyr Leu Thr Gly Glu Lys Gly Val Arg Val Glu Leu Asn Lys
            405   410   415

Pro Ser Asp Ser Val Gly Lys Asp Val Phe
            420   425

<210> 2577
<211> 346
<212> PRT
<213> Homo sapiens

989

<400> 2577

Met Glu Ser Val Ser Cys Ser Ala Ala Ala Val Arg Thr Gly Asp Met
1   5   10   15

Glu Ser Gln Arg Asp Leu Ser Leu Val Pro Glu Arg Leu Gln Arg Arg
            20   25   30

Glu Gln Glu Arg Gln Leu Glu Val Glu Arg Arg Lys Gln Lys Arg Gln
        35   40   45

Asn Gln Glu Val Glu Lys Glu Asn Ser His Phe Phe Val Ala Thr Phe
    50   55   60

Ala Arg Glu Arg Ala Ala Val Glu Glu Leu Leu Glu Arg Ala Glu Ser
65   70   75   80

Val Glu Arg Leu Glu Glu Ala Ala Ser Arg Leu Gln Gly Leu Gln Lys
            85   90   95

Leu Ile Asn Asp Ser Val Phe Phe Leu Ala Ala Tyr Asp Leu Arg Gln
            100   105   110

Gly Gln Glu Ala Leu Ala Arg Leu Gln Ala Ala Leu Ala Glu Arg Arg
        115   120   125

Arg Gly Leu Gln Pro Lys Lys Arg Phe Ala Phe Lys Thr Arg Gly Lys
        130   135   140

Asp Ala Ala Ser Ser Thr Lys Val Asp Ala Ala Pro Gly Ile Pro Pro
145   150   155   160

Ala Val Glu Ser Ile Gln Asp Ser Pro Leu Pro Lys Lys Ala Glu Gly
            165   170   175

Asp Leu Gly Pro Ser Trp Val Cys Gly Phe Ser Asn Leu Glu Ser Gln
            180   185   190

Val Leu Glu Lys Arg Ala Ser Glu Leu His Gln Arg Asp Val Leu Leu
        195   200   205

Thr Glu Leu Ser Asn Cys Thr Val Arg Leu Tyr Gly Asn Pro Asn Thr
    210   215   220

Leu Arg Leu Thr Lys Ala His Ser Cys Lys Leu Leu Cys Gly Pro Val
225   230   235   240

```
        Ser Thr Ser Val Phe Leu Glu Asp Cys Ser Asp Cys Val Leu Ala Val
                        245                 250                 255


        Ala Cys Gln Gln Leu Arg Ile His Ser Thr Lys Asp Thr Arg Ile Phe
                    260                 265                 270


        Leu Gln Val Thr Ser Arg Ala Ile Val Glu Asp Cys Ser Gly Ile Gln
                    275                 280                 285


        Phe Ala Pro Tyr Thr Trp Ser Tyr Pro Glu Ile Asp Lys Asp Phe Glu
                290                 295                 300


        Ser Ser Gly Leu Asp Arg Ser Lys Asn Asn Trp Asn Asp Val Asp Asp
        305                 310                 315                 320


        Phe Asn Trp Leu Ala Arg Asp Met Ala Ser Pro Asn Trp Ser Ile Leu
                        325                 330                 335


        Pro Glu Glu Glu Arg Asn Ile Gln Trp Asp
                        340                 345
```

```
        <210>   2578
        <211>   247
        <212>   PRT
        <213>   Homo sapiens

        <400>   2578
```

```
        Met Glu Phe Pro Lys Met Leu Thr Arg Lys Ile Lys Leu Trp Asp Ile
        1               5                   10                  15


        Asn Ala His Ile Thr Cys Arg Leu Cys Ser Gly Tyr Leu Ile Asp Ala
                        20                  25                  30


        Thr Thr Val Thr Glu Cys Leu His Thr Phe Cys Arg Ser Cys Leu Val
                    35                  40                  45


        Lys Tyr Leu Glu Glu Asn Asn Thr Cys Pro Thr Cys Arg Ile Val Ile
                50                  55                  60


        His Gln Ser His Pro Leu Gln Tyr Ile Gly His Asp Arg Thr Met Gln
        65                  70                  75                  80


        Asp Ile Val Tyr Lys Leu Val Pro Gly Leu Gln Glu Ala Glu Met Arg
                        85                  90                  95
```

```
Lys Gln Arg Glu Phe Tyr His Lys Leu Gly Met Glu Val Pro Gly Asp
            100                     105             110

Ile Lys Gly Glu Thr Cys Ser Ala Lys Gln His Leu Asp Ser His Arg
            115                 120             125

Asn Gly Glu Thr Lys Ala Asp Asp Ser Ser Asn Lys Glu Ala Ala Glu
    130                 135             140

Glu Lys Pro Glu Glu Asp Asn Asp Tyr His Arg Ser Asp Glu Gln Val
145                 150             155                 160

Ser Ile Cys Leu Glu Cys Asn Ser Ser Lys Leu Arg Gly Leu Lys Arg
                165             170             175

Lys Trp Ile Arg Cys Ser Ala Gln Ala Thr Val Leu His Leu Lys Lys
            180                 185             190

Phe Ile Ala Lys Lys Leu Asn Leu Ser Ser Phe Asn Glu Leu Asp Ile
        195                 200             205

Leu Cys Asn Glu Glu Ile Leu Gly Lys Asp His Thr Leu Lys Phe Val
    210                 215             220

Val Val Thr Arg Trp Arg Phe Lys Lys Ala Pro Leu Leu Leu His Tyr
225                 230             235                 240

Arg Pro Lys Met Asp Leu Leu
                245
```

```
<210>   2579
<211>   360
<212>   PRT
<213>   Homo sapiens

<400>   2579

Met Ala Ser Ala Thr Ala Pro Ala Ala Ala Val Pro Thr Leu Ala Ser
1               5               10              15

Pro Leu Glu Gln Leu Arg His Leu Ala Glu Glu Leu Arg Leu Leu Leu
            20              25              30

Pro Arg Val Arg Val Gly Glu Ala Gln Glu Thr Thr Glu Glu Phe Asn
        35              40              45

Arg Glu Met Phe Trp Arg Arg Leu Asn Glu Ala Ala Val Thr Val Ser
    50              55              60
```

```
Arg Glu Ala Thr Thr Leu Thr Ile Val Phe Ser Gln Leu Pro Leu Pro
65              70              75                  80


Ser Pro Gln Glu Thr Gln Lys Phe Cys Glu Gln Val His Ala Ala Ile
                85              90                  95


Lys Ala Phe Ile Ala Val Tyr Tyr Leu Leu Pro Lys Asp Gln Gly Ile
            100             105             110


Thr Leu Arg Lys Leu Val Arg Gly Ala Thr Leu Asp Ile Val Asp Gly
        115             120             125


Met Ala Gln Leu Met Glu Val Leu Ser Val Thr Pro Thr Gln Ser Pro
    130             135             140


Glu Asn Asn Asp Leu Ile Ser Tyr Asn Ser Val Trp Val Ala Cys Gln
145             150             155             160


Gln Met Pro Gln Ile Pro Arg Asp Asn Lys Ala Ala Ala Leu Leu Met
            165             170             175


Leu Thr Lys Asn Val Asp Phe Val Lys Asp Ala His Glu Glu Met Glu
        180             185             190


Gln Ala Val Glu Glu Cys Asp Pro Tyr Ser Gly Leu Leu Asn Asp Thr
        195             200             205


Glu Glu Asn Asn Ser Asp Asn His Asn His Glu Asp Asp Val Leu Gly
    210             215             220


Phe Pro Ser Asn Gln Asp Leu Tyr Trp Ser Glu Asp Asp Gln Glu Leu
225             230             235             240


Ile Ile Pro Cys Leu Ala Leu Val Arg Ala Ser Lys Ala Cys Leu Lys
            245             250             255


Lys Ile Arg Met Leu Val Ala Glu Asn Gly Lys Lys Asp Gln Val Ala
            260             265             270


Gln Met Ala Asp Ile Val Asp Ile Ser Asp Glu Ile Ser Pro Ser Val
        275             280             285


Asp Asp Leu Ala Leu Ser Ile Tyr Pro Pro Met Cys His Leu Thr Val
    290             295             300
```

993

Arg Ile Asn Ser Ala Lys Leu Val Ser Val Leu Lys Lys Ala Leu Glu
305   310   315   320

Ile Thr Lys Ala Ser His Val Thr Pro Gln Pro Glu Asp Ser Trp Ile
                325   330   335

Pro Leu Leu Ile Asn Ala Ile Asp His Cys Met Asn Arg Ile Lys Glu
            340   345   350

Leu Thr Gln Ser Glu Leu Glu Leu
        355   360

<210> 2580
<211> 412
<212> PRT
<213> Homo sapiens

<400> 2580

Met Ala Glu Asn Leu Lys Gly Cys Ser Val Cys Cys Lys Ser Ser Trp
1   5   10   15

Asn Gln Leu Gln Asp Leu Cys Arg Leu Ala Lys Leu Ser Cys Pro Ala
            20   25   30

Leu Gly Ile Ser Lys Arg Asn Leu Tyr Asp Phe Glu Val Glu Tyr Leu
            35   40   45

Cys Asp Tyr Lys Lys Ile Arg Glu Gln Glu Tyr Tyr Leu Val Lys Trp
        50   55   60

Arg Gly Tyr Pro Asp Ser Glu Ser Thr Trp Glu Pro Arg Gln Asn Leu
65   70   75   80

Lys Cys Val Arg Ile Leu Lys Gln Phe His Lys Asp Leu Glu Arg Glu
                85   90   95

Leu Leu Arg Arg His His Arg Ser Lys Thr Pro Arg His Leu Asp Pro
            100   105   110

Ser Leu Ala Asn Tyr Leu Val Gln Lys Ala Lys Gln Arg Arg Ala Leu
        115   120   125

Arg Arg Trp Glu Gln Glu Leu Asn Ala Lys Arg Ser His Leu Gly Arg
        130   135   140

Ile Thr Val Glu Asn Glu Val Asp Leu Asp Gly Pro Pro Arg Ala Phe

994

145   150   155   160

Val Tyr Ile Asn Glu Tyr Arg Val Gly Glu Gly Ile Thr Leu Asn Gln
              165   170   175

Val Ala Val Gly Cys Glu Cys Gln Asp Cys Leu Trp Ala Pro Thr Gly
              180   185   190

Gly Cys Cys Pro Gly Ala Ser Leu His Lys Phe Ala Tyr Asn Asp Gln
          195   200   205

Gly Gln Val Arg Leu Arg Ala Gly Leu Pro Ile Tyr Glu Cys Asn Ser
      210   215   220

Arg Cys Arg Cys Gly Tyr Asp Cys Pro Asn Arg Val Val Gln Lys Gly
225   230   235   240

Ile Arg Tyr Asp Leu Cys Ile Phe Arg Thr Asp Asp Gly Arg Gly Trp
              245   250   255

Gly Val Arg Thr Leu Glu Lys Ile Arg Lys Asn Ser Phe Val Met Glu
              260   265   270

Tyr Val Gly Glu Ile Ile Thr Ser Glu Glu Ala Glu Arg Arg Gly Gln
          275   280   285

Ile Tyr Asp Arg Gln Gly Ala Thr Tyr Leu Phe Asp Leu Asp Tyr Val
      290   295   300

Glu Asp Val Tyr Thr Val Asp Ala Ala Tyr Tyr Gly Asn Ile Ser His
305   310   315   320

Phe Val Asn His Ser Cys Asp Pro Asn Leu Gln Val Tyr Asn Val Phe
              325   330   335

Ile Asp Asn Leu Asp Glu Arg Leu Pro Arg Ile Ala Phe Phe Ala Thr
              340   345   350

Arg Thr Ile Arg Ala Gly Glu Glu Leu Thr Phe Asp Tyr Asn Met Gln
          355   360   365

Val Asp Pro Val Asp Met Glu Ser Thr Arg Met Asp Ser Asn Phe Gly
      370   375   380

Leu Ala Gly Leu Pro Gly Ser Pro Lys Lys Arg Val Arg Ile Glu Cys
385   390   395   400

```
Lys Cys Gly Thr Glu Ser Cys Arg Lys Tyr Leu Phe
                405                 410
```

```
<210>  2581
<211>  110
<212>  PRT
<213>  Homo sapiens

<400>  2581
```

```
Met Val Tyr Glu Arg Ala Gly Glu Ala Val Pro Pro Arg Gly Leu Arg
1               5                 10              15
```

```
Glu Lys Phe Pro Arg Ala Leu Phe Gly Trp Ala Gly Glu Arg Pro Ser
            20                25              30
```

```
Ala Leu Cys Ala Ser Asn Pro Pro Gln Leu Ser Cys Ser Gly Arg Gly
        35              40              45
```

```
Ala Arg Tyr Phe Arg Leu Gly Glu Val Leu Gly Thr Asp Val Gly Ser
    50              55              60
```

```
Ser Val Gly Asp Phe Ser Gly Phe Trp Pro Phe Gln Thr Leu Val Ile
65              70              75                  80
```

```
Val Phe Ser Val Gln Ser Ser Phe Gly Val Trp Gly Phe Pro Ser Ser
            85              90              95
```

```
Cys Ala Arg His Arg Glu Ala Trp Pro Glu Gly Pro Val Ser
            100             105             110
```

```
<210>  2582
<211>  471
<212>  PRT
<213>  Homo sapiens

<400>  2582
```

```
Met Pro Asn Ser Glu Pro Ala Ser Leu Leu Glu Leu Phe Asn Ser Ile
1               5                 10              15
```

```
Ala Thr Gln Gly Glu Leu Val Arg Ser Leu Lys Ala Gly Asn Ala Ser
            20                25              30
```

```
Lys Asp Glu Ile Asp Ser Ala Val Lys Met Leu Val Ser Leu Lys Met
        35              40              45
```

```
Ser Tyr Lys Ala Ala Ala Gly Glu Asp Tyr Lys Ala Asp Cys Pro Pro
```

```
          50                    55                    60


Gly Asn Pro Ala Pro Thr Ser Asn His Gly Pro Asp Ala Thr Glu Ala
65              70              75              80


Glu Glu Asp Phe Val Asp Pro Trp Thr Val Gln Thr Ser Ser Ala Lys
                85              90              95


Gly Ile Asp Tyr Asp Lys Leu Ile Val Arg Phe Gly Ser Ser Lys Ile
                100             105             110


Asp Lys Glu Leu Ile Asn Arg Ile Glu Arg Ala Thr Gly Gln Arg Pro
        115             120             125


His His Phe Leu Arg Arg Gly Ile Phe Phe Ser His Arg Asp Met Asn
    130             135             140


Gln Val Leu Asp Ala Tyr Glu Asn Lys Lys Pro Phe Tyr Leu Tyr Thr
145             150             155             160


Gly Arg Gly Pro Ser Ser Glu Ala Met His Val Gly His Leu Ile Pro
                165             170             175


Phe Ile Phe Thr Lys Trp Leu Gln Asp Val Phe Asn Val Pro Leu Val
            180             185             190


Ile Gln Met Thr Asp Asp Glu Lys Tyr Leu Trp Lys Asp Leu Thr Leu
            195             200             205


Asp Gln Ala Tyr Gly Asp Ala Val Glu Asn Ala Lys Asp Ile Ile Ala
    210             215             220


Cys Gly Phe Asp Ile Asn Lys Thr Phe Ile Phe Ser Asp Leu Asp Tyr
225             230             235             240


Met Gly Met Ser Ser Gly Phe Tyr Lys Asn Val Val Lys Ile Gln Lys
                245             250             255


His Val Thr Phe Asn Gln Val Lys Gly Ile Phe Gly Phe Thr Asp Ser
            260             265             270


Asp Cys Ile Gly Lys Ile Ser Phe Pro Ala Ile Gln Ala Ala Pro Ser
        275             280             285


Phe Ser Asn Ser Phe Pro Gln Ile Phe Arg Asp Arg Thr Asp Ile Gln
    290             295             300
```

```
Cys Leu Ile Pro Cys Ala Ile Asp Gln Asp Pro Tyr Phe Arg Met Thr
305                 310                 315                 320


Arg Asp Val Ala Pro Arg Ile Gly Tyr Pro Lys Pro Ala Leu Leu His
            325                 330                 335


Ser Thr Phe Phe Pro Ala Leu Gln Gly Ala Gln Thr Lys Met Ser Ala
            340                 345                 350


Ser Asp Pro Asn Ser Ser Ile Phe Leu Thr Asp Thr Ala Lys Gln Ile
        355                 360                 365


Lys Thr Lys Val Asn Lys His Ala Phe Ser Gly Gly Arg Asp Thr Ile
    370                 375                 380


Glu Glu His Arg Gln Phe Gly Gly Asn Cys Asp Val Asp Val Ser Phe
385                 390                 395                 400


Met Tyr Leu Thr Phe Phe Leu Glu Asp Asp Asp Lys Leu Glu Gln Ile
            405                 410                 415


Arg Lys Asp Tyr Thr Ser Gly Ala Met Leu Thr Gly Glu Leu Lys Lys
            420                 425                 430


Ala Leu Ile Glu Val Leu Gln Pro Leu Ile Ala Glu His Gln Ala Arg
        435                 440                 445


Arg Lys Glu Val Thr Asp Glu Ile Val Lys Glu Phe Met Thr Pro Arg
    450                 455                 460


Lys Leu Ser Phe Asp Phe Gln
465                 470


<210>  2583
<211>  392
<212>  PRT
<213>  Homo sapiens

<400>  2583

Met Gly Ser Leu Ser Thr Ala Asn Val Glu Phe Cys Leu Asp Val Phe
1               5                   10                  15


Lys Glu Leu Asn Ser Asn Asn Ile Gly Asp Asn Ile Phe Phe Ser Ser
            20                  25                  30
```

```
Leu Ser Leu Leu Tyr Ala Leu Ser Met Val Leu Leu Gly Ala Arg Gly
        35              40              45

Glu Thr Ala Glu Gln Leu Glu Lys Val Leu His Phe Ser His Thr Val
    50              55              60

Asp Ser Leu Lys Pro Gly Phe Lys Asp Ser Pro Lys Cys Ser Gln Ala
65              70              75              80

Gly Arg Ile His Ser Glu Phe Gly Val Glu Phe Ser Gln Ile Asn Gln
                85              90              95

Pro Asp Ser Asn Cys Thr Leu Ser Ile Ala Asn Arg Leu Tyr Gly Thr
            100             105             110

Lys Thr Met Ala Phe His Gln Gln Tyr Leu Ser Cys Ser Glu Lys Trp
        115             120             125

Tyr Gln Ala Arg Leu Gln Thr Val Asp Phe Glu Gln Ser Thr Glu Glu
    130             135             140

Thr Arg Lys Met Ile Asn Ala Trp Val Glu Asn Lys Thr Asn Gly Lys
145             150             155             160

Val Ala Asn Leu Phe Gly Lys Ser Thr Ile Asp Pro Ser Ser Val Met
            165             170             175

Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Gln Arg Gln Asn Lys Phe
            180             185             190

Gln Val Arg Glu Thr Val Lys Ser Pro Phe Gln Leu Ser Glu Gly Lys
        195             200             205

Asn Val Thr Val Glu Met Met Tyr Gln Ile Gly Thr Phe Lys Leu Ala
    210             215             220

Phe Val Lys Glu Pro Gln Met Gln Val Leu Glu Leu Pro Tyr Val Asn
225             230             235             240

Asn Lys Leu Ser Met Ile Ile Leu Leu Pro Val Gly Ile Ala Asn Leu
            245             250             255

Lys Gln Ile Glu Lys Gln Leu Asn Ser Gly Thr Phe His Glu Trp Thr
        260             265             270

Ser Ser Ser Asn Met Met Glu Arg Glu Val Glu Val His Leu Pro Arg
```

999

```
            275                    280                    285


     Phe Lys Leu Glu Ile Lys Tyr Glu Leu Asn Ser Leu Leu Lys Pro Leu
         290                    295                300


     Gly Val Thr Asp Leu Phe Asn Gln Val Lys Ala Asp Leu Ser Gly Met
     305                    310                315                320


     Ser Pro Thr Lys Gly Leu Tyr Leu Ser Lys Ala Ile His Lys Ser Tyr
                     325                330                335


     Leu Asp Val Ser Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Gly Asp
                     340                345                350


     Ser Ile Ala Val Lys Ser Leu Pro Met Arg Ala Gln Phe Lys Ala Asn
                 355                360                365


     His Pro Phe Leu Phe Phe Ile Arg His Thr His Thr Asn Thr Ile Leu
         370                    375                380


     Phe Cys Gly Lys Leu Ala Ser Pro
     385                    390


     <210> 2584
     <211> 811
     <212> PRT
     <213> Homo sapiens

     <400> 2584

     Met Pro Leu Ser Ser Pro Asn Ala Ala Ala Thr Ala Ser Asp Met Asp
     1               5                  10                 15


     Lys Asn Ser Gly Ser Asn Ser Ser Ser Ala Ser Ser Gly Ser Ser Lys
                     20                 25                 30


     Gly Gln Gln Pro Pro Arg Ser Ala Ser Ala Gly Pro Ala Gly Glu Ser
                 35                 40                 45


     Lys Pro Lys Ser Asp Gly Lys Asn Ser Ser Gly Ser Lys Arg Tyr Asn
         50                 55                 60


     Arg Lys Arg Glu Leu Ser Tyr Pro Lys Asn Glu Ser Phe Asn Asn Gln
     65                 70                 75                 80


     Ser Arg Arg Ser Ser Ser Gln Lys Ser Lys Thr Phe Asn Lys Met Pro
                     85                 90                 95
```

```
Pro Gln Arg Gly Gly Gly Ser Ser Lys Leu Phe Ser Ser Ser Phe Asn
            100                 105                 110


Gly Gly Arg Arg Asp Glu Val Ala Glu Ala Gln Arg Ala Glu Phe Ser
            115                 120                 125


Pro Ala Gln Phe Ser Gly Pro Lys Lys Ile Asn Leu Asn His Leu Leu
    130                 135                 140


Asn Phe Thr Phe Glu Pro Arg Gly Gln Thr Gly His Phe Glu Gly Ser
145                 150                 155                 160


Gly His Gly Ser Trp Gly Lys Arg Asn Lys Trp Gly His Lys Pro Phe
                165                 170                 175


Asn Lys Glu Leu Phe Leu Gln Ala Asn Cys Gln Phe Val Val Ser Glu
            180                 185                 190


Asp Gln Asp Tyr Thr Ala His Phe Ala Asp Pro Asp Thr Leu Val Asn
            195                 200                 205


Trp Asp Phe Val Glu Gln Val Arg Ile Cys Ser His Glu Val Pro Ser
    210                 215                 220


Cys Pro Ile Cys Leu Tyr Pro Pro Thr Ala Ala Lys Ile Thr Arg Cys
225                 230                 235                 240


Gly His Ile Phe Cys Trp Ala Cys Ile Leu His Tyr Leu Ser Leu Ser
                245                 250                 255


Glu Lys Thr Trp Ser Lys Cys Pro Ile Cys Tyr Ser Ser Val His Lys
            260                 265                 270


Lys Asp Leu Lys Ser Val Val Ala Thr Glu Ser His Gln Tyr Val Val
            275                 280                 285


Gly Asp Thr Ile Thr Met Gln Leu Met Lys Arg Glu Lys Gly Val Leu
    290                 295                 300


Val Ala Leu Pro Lys Ser Lys Trp Met Asn Val Asp His Pro Ile His
305                 310                 315                 320


Leu Gly Asp Glu Gln His Ser Gln Tyr Ser Lys Phe Leu Leu Ala Ser
                325                 330                 335
```

Lys Glu Gln Val Leu His Arg Val Val Leu Glu Glu Lys Val Ala Leu
          340   345   350

Glu Gln Gln Leu Ala Glu Glu Lys His Thr Pro Glu Ser Cys Phe Ile
          355   360   365

Glu Ala Ala Ile Gln Glu Leu Lys Thr Arg Glu Glu Ala Leu Ser Gly
          370   375   380

Leu Ala Gly Ser Arg Arg Glu Val Thr Gly Val Val Ala Ala Leu Glu
385   390   395   400

Gln Leu Val Leu Met Ala Pro Leu Ala Lys Glu Ser Val Phe Gln Pro
                    405   410   415

Arg Lys Gly Val Leu Glu Tyr Leu Ser Ala Phe Asp Glu Glu Thr Thr
              420   425   430

Glu Val Cys Ser Leu Asp Thr Pro Ser Arg Pro Leu Ala Leu Pro Leu
          435   440   445

Val Glu Glu Glu Glu Ala Val Ser Glu Pro Glu Pro Glu Gly Leu Pro
          450   455   460

Glu Ala Cys Asp Asp Leu Glu Leu Ala Asp Asp Asn Leu Lys Glu Gly
465   470   475   480

Thr Ile Cys Thr Glu Ser Ser Gln Gln Glu Pro Ile Thr Lys Ser Gly
              485   490   495

Phe Thr Arg Leu Ser Ser Ser Pro Cys Tyr Tyr Phe Tyr Gln Ala Glu
          500   505   510

Asp Gly Gln His Met Phe Leu His Pro Val Asn Val Arg Cys Leu Val
          515   520   525

Arg Glu Tyr Gly Ser Leu Glu Arg Ser Pro Glu Lys Ile Ser Ala Thr
          530   535   540

Val Val Glu Ile Ala Gly Tyr Ser Met Ser Glu Asp Val Arg Gln Arg
545   550   555   560

His Arg Tyr Leu Ser His Leu Pro Leu Thr Cys Glu Phe Ser Ile Cys
              565   570   575

Glu Leu Ala Leu Gln Pro Pro Val Val Ser Lys Glu Thr Leu Glu Met

```
              580                      585                      590
```

Phe Ser Asp Asp Ile Glu Lys Arg Lys Arg Gln Arg Gln Lys Lys Ala
        595   600   605

Arg Glu Glu Arg Arg Arg Glu Arg Arg Ile Glu Ile Glu Glu Asn Lys
    610   615   620

Lys Gln Gly Lys Tyr Pro Glu Val His Ile Pro Leu Glu Asn Leu Gln
625   630   635   640

Gln Phe Pro Ala Phe Asn Ser Tyr Thr Cys Ser Ser Asp Ser Ala Leu
            645   650   655

Gly Pro Thr Ser Thr Glu Gly His Gly Ala Leu Ser Ile Ser Pro Leu
            660   665   670

Ser Arg Ser Pro Gly Ser His Ala Asp Phe Leu Leu Thr Pro Leu Ser
    675   680   685

Pro Thr Ala Ser Gln Gly Ser Pro Ser Phe Cys Val Gly Ser Leu Glu
    690   695   700

Glu Asp Ser Pro Phe Pro Ser Phe Ala Gln Met Leu Arg Val Gly Lys
705   710   715   720

Ala Lys Ala Asp Val Trp Pro Lys Thr Ala Pro Lys Lys Asp Glu Asn
            725   730   735

Ser Leu Val Pro Pro Ala Pro Val Asp Ser Asp Gly Glu Ser Asp Asn
            740   745   750

Ser Asp Arg Val Pro Val Pro Ser Phe Gln Asn Ser Phe Ser Gln Ala
    755   760   765

Ile Glu Ala Ala Phe Met Lys Leu Asp Thr Pro Ala Thr Ser Asp Pro
770   775   780

Leu Ser Glu Glu Lys Gly Gly Lys Lys Arg Lys Lys Gln Lys Gln Lys
785   790   795   800

Leu Leu Phe Ser Thr Ser Val Val His Thr Lys
            805   810

<210>   2585
<211>   482

<212>   PRT
<213>   Homo sapiens

<400>   2585

Met Ala Glu Ala Ala Thr Pro Gly Thr Thr Ala Thr Thr Ser Gly Ala
1   5   10   15

Gly Ala Ala Ala Ala Thr Ala Ala Ala Ser Pro Thr Pro Ile Pro
        20   25   30

Thr Val Thr Ala Pro Ser Leu Gly Ala Gly Gly Gly Gly Gly Ser
        35   40   45

Asp Gly Ser Gly Gly Gly Trp Thr Lys Gln Val Thr Cys Arg Tyr Phe
    50   55   60

Met His Gly Val Cys Lys Glu Gly Asp Asn Cys Arg Tyr Ser His Asp
65   70   75   80

Leu Ser Asp Ser Pro Tyr Ser Val Val Cys Lys Tyr Phe Gln Arg Gly
                85   90   95

Tyr Cys Ile Tyr Gly Asp Arg Cys Arg Tyr Glu His Ser Lys Pro Leu
            100   105   110

Lys Gln Glu Glu Ala Thr Ala Thr Glu Leu Thr Thr Lys Ser Ser Leu
        115   120   125

Ala Ala Ser Ser Ser Leu Ser Ser Ile Val Gly Pro Leu Val Glu Met
    130   135   140

Asn Thr Gly Glu Ala Glu Ser Arg Asn Ser Asn Phe Ala Thr Val Gly
145   150   155   160

Ala Gly Ser Glu Asp Trp Val Asn Ala Ile Glu Phe Val Pro Gly Gln
            165   170   175

Pro Tyr Cys Gly Arg Thr Ala Pro Ser Cys Thr Glu Ala Pro Leu Gln
        180   185   190

Gly Ser Val Thr Lys Glu Glu Ser Glu Lys Glu Gln Thr Ala Val Glu
        195   200   205

Thr Lys Lys Gln Leu Cys Pro Tyr Ala Ala Val Gly Glu Cys Arg Tyr
210   215   220

1004

Gly Glu Asn Cys Val Tyr Leu His Gly Asp Ser Cys Asp Met Cys Gly
225   230   235   240

Leu Gln Leu Leu His Pro Met Asp Ala Ala Gln Arg Ser Gln His Ile
            245   250   255

Lys Ser Cys Ile Glu Ala His Glu Lys Asp Met Glu Leu Ser Phe Ala
            260   265   270

Val Gln Arg Ser Lys Asp Met Val Cys Gly Ile Cys Met Glu Val Val
        275   280   285

Tyr Glu Lys Ala Asn Pro Ser Glu Arg Arg Phe Gly Ile Leu Ser Asn
    290   295   300

Cys Asn His Thr Tyr Cys Leu Lys Cys Ile Arg Lys Trp Arg Ser Ala
305   310   315   320

Lys Gln Phe Glu Ser Lys Ile Ile Lys Ser Cys Pro Glu Cys Arg Ile
            325   330   335

Thr Ser Asn Phe Val Ile Pro Ser Glu Tyr Trp Val Glu Glu Lys Glu
        340   345   350

Glu Lys Gln Lys Leu Ile Leu Lys Tyr Lys Glu Ala Met Ser Asn Lys
    355   360   365

Ala Cys Arg Tyr Phe Asp Glu Gly Arg Gly Ser Cys Pro Phe Gly Gly
    370   375   380

Asn Cys Phe Tyr Lys His Ala Tyr Pro Asp Gly Arg Arg Glu Glu Pro
385   390   395   400

Gln Arg Gln Lys Val Gly Thr Ser Ser Arg Tyr Arg Ala Gln Arg Arg
            405   410   415

Asn His Phe Trp Glu Leu Ile Glu Glu Arg Glu Asn Ser Asn Pro Phe
            420   425   430

Asp Asn Asp Glu Glu Glu Val Val Thr Phe Glu Leu Gly Glu Met Leu
        435   440   445

Leu Met Leu Leu Ala Ala Gly Gly Asp Asp Glu Leu Thr Asp Ser Glu
450   455   460

Asp Glu Trp Asp Leu Phe His Asp Glu Leu Glu Asp Phe Tyr Asp Leu

1005

465   470   475   480

Asp Leu

<210> 2586
<211> 146
<212> PRT
<213> Homo sapiens

<400> 2586

Met Pro Ser Lys Gly Pro Leu Gln Ser Val Gln Val Phe Gly Arg Lys
1   5   10   15

Lys Thr Ala Thr Ala Val Ala His Cys Lys Arg Gly Asn Gly Leu Ile
            20   25   30

Lys Val Asn Gly Arg Pro Leu Glu Met Ile Glu Pro Arg Thr Leu Gln
        35   40   45

Tyr Lys Leu Leu Glu Pro Val Leu Leu Leu Gly Lys Glu Arg Phe Ala
    50   55   60

Gly Val Asp Ile Arg Val Arg Val Lys Gly Gly Gly His Val Ala Gln
65   70   75   80

Ile Tyr Ala Ile Arg Gln Ser Ile Ser Lys Ala Leu Val Ala Tyr Tyr
                85   90   95

Gln Lys Tyr Val Asp Glu Ala Ser Lys Lys Glu Ile Lys Asp Ile Leu
            100   105   110

Ile Gln Tyr Asp Arg Thr Leu Leu Val Ala Asp Pro Arg Arg Cys Glu
        115   120   125

Ser Lys Lys Phe Gly Gly Pro Gly Ala Arg Ala Arg Tyr Gln Lys Ser
    130   135   140

Tyr Arg
145

<210> 2587
<211> 1674
<212> PRT
<213> Homo sapiens

<400> 2587

```
Met Glu Asp Ala Ser Glu Ser Ser Arg Gly Val Ala Pro Leu Ile Asn
1               5                   10                  15

Asn Val Val Leu Pro Gly Ser Pro Leu Ser Leu Pro Val Ser Val Thr
            20                  25                  30

Gly Cys Lys Ser His Arg Val Ala Asn Lys Lys Val Glu Ala Arg Ser
        35                  40                  45

Glu Lys Leu Leu Pro Thr Ala Leu Pro Pro Ser Glu Pro Lys Val Asp
    50                  55                  60

Gln Lys Leu Pro Arg Ser Ser Glu Arg Arg Gly Ser Gly Gly Gly Thr
65                  70                  75                  80

Gln Phe Pro Ala Arg Ser Arg Ala Val Ala Ala Gly Glu Ala Ala Ala
            85                  90                  95

Arg Gly Ala Ala Gly Pro Glu Arg Gly Ser Pro Leu Gly Arg Arg Val
        100                 105                 110

Ser Pro Arg Cys Leu Cys Ser Gly Glu Gly Gly Gln Val Ala Val Gly
    115                 120                 125

Val Ile Ala Gly Lys Arg Gly Arg Arg Gly Arg Asp Gly Ser Arg Arg
    130                 135                 140

Ala Pro Gly Gly Arg Glu Met Pro Leu Leu His Arg Lys Pro Phe Val
145                 150                 155                 160

Arg Gln Lys Pro Pro Ala Asp Leu Arg Pro Asp Glu Glu Val Phe Tyr
            165                 170                 175

Cys Lys Val Thr Asn Glu Ile Phe Arg His Tyr Asp Asp Phe Phe Glu
            180                 185                 190

Arg Thr Ile Leu Cys Asn Ser Leu Val Trp Ser Cys Ala Val Thr Gly
        195                 200                 205

Arg Pro Gly Leu Thr Tyr Gln Glu Ala Leu Glu Ser Glu Lys Lys Ala
    210                 215                 220

Arg Gln Asn Leu Gln Ser Phe Pro Glu Pro Leu Ile Ile Pro Val Leu
225                 230                 235                 240

Tyr Leu Thr Ser Leu Thr His Arg Ser Arg Leu His Glu Ile Cys Asp
```

```
                    245                    250                    255


Asp Ile Phe Ala Tyr Val Lys Asp Arg Tyr Phe Val Glu Glu Thr Val
            260                 265                 270


Glu Val Ile Arg Asn Asn Gly Ala Arg Leu Gln Cys Thr Ile Leu Glu
            275                 280                 285


Val Leu Pro Pro Ser His Gln Asn Gly Phe Ala Asn Gly His Val Asn
    290                 295                 300


Ser Val Asp Gly Glu Thr Ile Ile Ile Ser Asp Ser Asp Asp Ser Glu
305                 310                 315                 320


Thr Gln Ser Cys Ser Phe Gln Asn Gly Lys Lys Lys Asp Ala Ile Asp
            325                 330                 335


Pro Leu Leu Phe Lys Tyr Lys Val Gln Pro Thr Lys Lys Glu Leu His
            340                 345                 350


Glu Ser Ala Ile Val Lys Ala Thr Gln Ile Ser Arg Arg Lys His Leu
            355                 360                 365


Phe Ser Arg Asp Lys Leu Lys Leu Phe Leu Lys Gln His Cys Glu Pro
    370                 375                 380


Gln Glu Gly Val Ile Lys Ile Lys Ala Ser Ser Leu Ser Thr Tyr Lys
385                 390                 395                 400


Ile Ala Glu Gln Asp Phe Ser Tyr Phe Phe Pro Asp Asp Pro Pro Thr
                405                 410                 415


Phe Ile Phe Ser Pro Ala Asn Arg Arg Arg Gly Arg Pro Pro Lys Arg
            420                 425                 430


Ile His Ile Ser Gln Glu Asp Asn Val Ala Asn Lys Gln Thr Leu Ala
            435                 440                 445


Ser Tyr Arg Ser Lys Ala Thr Lys Glu Arg Asp Lys Leu Leu Lys Gln
    450                 455                 460


Glu Glu Met Lys Ser Leu Ala Phe Glu Lys Ala Lys Leu Lys Arg Glu
465                 470                 475                 480


Lys Ala Asp Ala Leu Glu Ala Lys Lys Lys Glu Lys Glu Asp Lys Glu
                485                 490                 495
```

```
Lys Lys Arg Glu Glu Leu Lys Lys Ile Val Glu Glu Glu Arg Leu Lys
            500                 505                 510

Lys Lys Glu Glu Lys Glu Arg Leu Lys Val Glu Arg Glu Lys Glu Arg
            515                 520                 525

Glu Lys Leu Arg Glu Glu Lys Arg Lys Tyr Val Glu Tyr Leu Lys Gln
    530                 535                 540

Trp Ser Lys Pro Arg Glu Asp Met Glu Cys Asp Asp Leu Lys Glu Leu
545                 550                 555                 560

Pro Glu Pro Thr Pro Val Lys Thr Arg Leu Pro Pro Glu Ile Phe Gly
                565                 570                 575

Asp Ala Leu Met Val Leu Glu Phe Leu Asn Ala Phe Gly Glu Leu Phe
            580                 585                 590

Asp Leu Gln Asp Glu Phe Pro Asp Gly Val Thr Leu Glu Val Leu Glu
    595                 600                 605

Glu Ala Leu Val Gly Asn Asp Ser Glu Gly Pro Leu Cys Glu Leu Leu
    610                 615                 620

Phe Phe Phe Leu Thr Ala Ile Phe Gln Ala Ile Ala Glu Glu Glu Glu
625                 630                 635                 640

Glu Val Ala Lys Glu Gln Leu Thr Asp Ala Asp Thr Lys Gly Cys Ser
                645                 650                 655

Leu Lys Ser Leu Asp Leu Asp Ser Cys Thr Leu Ser Glu Ile Leu Arg
                660                 665                 670

Leu His Ile Leu Ala Ser Gly Ala Asp Val Thr Ser Ala Asn Ala Lys
            675                 680                 685

Tyr Arg Tyr Gln Lys Arg Gly Gly Phe Asp Ala Thr Asp Asp Ala Cys
    690                 695                 700

Met Glu Leu Arg Leu Ser Asn Pro Ser Leu Val Lys Lys Leu Ser Ser
705                 710                 715                 720

Thr Ser Val Tyr Asp Leu Thr Pro Gly Glu Lys Met Lys Ile Leu His
                725                 730                 735
```

```
Ala Leu Cys Gly Lys Leu Leu Thr Leu Val Ser Thr Arg Asp Phe Ile
            740                 745                 750

Glu Asp Tyr Val Asp Ile Leu Arg Gln Ala Lys Gln Glu Phe Arg Glu
            755                 760                 765

Leu Lys Ala Glu Gln His Arg Lys Glu Arg Glu Glu Ala Ala Ala Arg
    770                 775                 780

Ile Arg Lys Arg Lys Glu Glu Lys Leu Lys Glu Gln Glu Gln Lys Met
785                 790                 795                 800

Lys Glu Lys Gln Glu Lys Leu Lys Glu Asp Glu Gln Arg Asn Ser Thr
                805                 810                 815

Ala Asp Ile Ser Ile Gly Glu Glu Glu Arg Glu Asp Phe Asp Thr Ser
            820                 825                 830

Ile Glu Ser Lys Asp Thr Glu Gln Lys Glu Leu Asp Gln Asp Met Phe
            835                 840                 845

Thr Glu Asp Glu Asp Asp Pro Gly Ser His Lys Arg Gly Arg Arg Gly
    850                 855                 860

Lys Arg Gly Gln Asn Gly Phe Lys Glu Phe Thr Arg Gln Glu Gln Ile
865                 870                 875                 880

Asn Cys Val Thr Arg Glu Leu Leu Thr Ala Asp Glu Glu Glu Ala Leu
            885                 890                 895

Lys Gln Glu His Gln Arg Lys Glu Lys Glu Leu Leu Glu Lys Ile Gln
            900                 905                 910

Ser Ala Ile Ala Cys Thr Asn Ile Phe Pro Leu Gly Arg Asp Arg Met
    915                 920                 925

Tyr Arg Arg Tyr Trp Ile Phe Pro Ser Ile Pro Gly Leu Phe Ile Glu
    930                 935                 940

Glu Asp Tyr Ser Gly Leu Thr Glu Asp Met Leu Leu Pro Arg Pro Ser
945                 950                 955                 960

Ser Phe Gln Asn Asn Val Gln Ser Gln Asp Pro Gln Val Ser Thr Lys
                965                 970                 975
```

1010

```
Thr Gly Glu Pro Leu Met Ser Glu Ser Thr Ser Asn Ile Asp Gln Gly
        980                 985             990


Pro Arg Asp His Ser Val Gln Leu  Pro Lys Pro Val His  Lys Pro Asn
        995             1000             1005


Arg Trp Cys Phe Tyr Ser Ser Cys Glu Gln Leu Asp Gln Leu Ile
    1010         1015         1020


Glu Ala Leu Asn Ser Arg Gly His Arg Glu Ser Ala Leu Lys Glu
    1025         1030         1035


Thr Leu Leu Gln Glu Lys Ser Arg Ile Cys Ala Gln Leu Ala Arg
    1040         1045         1050


Phe Ser Glu Glu Lys Phe His Phe Ser Asp Lys Pro Gln Pro Asp
    1055         1060         1065


Ser Lys Pro Thr Tyr Ser Arg Gly Arg Ser Ser Asn Ala Tyr Asp
    1070         1075         1080


Pro Ser Gln Met Cys Ala Glu Lys Gln Leu Glu Leu Arg Leu Arg
    1085         1090         1095


Asp Phe Leu Leu Asp Ile Glu Asp Arg Ile Tyr Gln Gly Thr Leu
    1100         1105         1110


Gly Ala Ile Lys Val Thr Asp Arg His Ile Trp Arg Ser Ala Leu
    1115         1120         1125


Glu Ser Gly Arg Tyr Glu Leu Leu Ser Glu Glu Asn Lys Glu Asn
    1130         1135         1140


Gly Ile Ile Lys Thr Val Asn Glu Asp Val Glu Glu Met Glu Ile
    1145         1150         1155


Asp Glu Gln Thr Lys Val Ile Val Lys Asp Arg Leu Leu Gly Ile
    1160         1165         1170


Lys Thr Glu Thr Pro Ser Thr Val Ser Thr Asn Ala Ser Thr Pro
    1175         1180         1185


Gln Ser Val Ser Ser Val Val His Tyr Leu Ala Met Ala Leu Phe
    1190         1195         1200


Gln Ile Glu Gln Gly Ile Glu Arg Arg Phe Leu Lys Ala Pro Leu
```

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        1205                    1210                      1215


 Asp Ala  Ser Asp Ser Gly Arg  Ser Tyr Lys Thr Val  Leu Asp Arg
     1220             1225               1230


 Trp Arg  Glu Ser Leu Leu Ser  Ser Ala Ser Leu Ser  Gln Val Phe
     1235             1240               1245


 Leu His  Leu Ser Thr Leu Asp  Arg Ser Val Ile Trp  Ser Lys Ser
     1250             1255               1260


 Ile Leu  Asn Ala Arg Cys Lys  Ile Cys Arg Lys Lys  Gly Asp Ala
     1265             1270               1275


 Glu Asn  Met Val Leu Cys Asp  Gly Cys Asp Arg Gly  His His Thr
     1280             1285               1290


 Tyr Cys  Val Arg Pro Lys Leu  Lys Thr Val Pro Glu  Gly Asp Trp
     1295             1300               1305


 Phe Cys  Pro Glu Cys Arg Pro  Lys Gln Arg Cys Arg  Arg Leu Ser
     1310             1315               1320


 Phe Arg  Gln Arg Pro Ser Leu  Glu Ser Asp Glu Asp  Val Glu Asp
     1325             1330               1335


 Ser Met  Gly Gly Glu Asp Asp  Glu Val Asp Gly Asp  Glu Glu Glu
     1340             1345               1350


 Gly Gln  Ser Glu Glu Glu Glu  Tyr Glu Val Glu Gln  Asp Glu Asp
     1355             1360               1365


 Asp Ser  Gln Glu Glu Glu Glu  Val Ser Leu Pro Lys  Arg Gly Arg
     1370             1375               1380


 Pro Gln  Val Arg Leu Pro Val  Lys Thr Arg Gly Lys  Leu Ser Ser
     1385             1390               1395


 Ser Phe  Ser Ser Arg Gly Gln  Gln Gln Glu Pro Gly  Arg Tyr Pro
     1400             1405               1410


 Ser Arg  Ser Gln Gln Ser Thr  Pro Lys Thr Thr Val  Ser Ser Lys
     1415             1420               1425


 Thr Gly  Arg Ser Leu Arg Lys  Ile Asn Ser Ala Pro  Pro Thr Glu
     1430             1435               1440
```

```
Thr Lys  Ser Leu Arg Ile Ala  Ser Arg Ser Thr Arg  His Ser His
    1445                 1450                 1455


Gly Pro  Leu Gln Ala Asp Val  Phe Val Glu Leu Leu  Ser Pro Arg
    1460                 1465                 1470
    .


Arg Lys  Arg Arg Gly Arg Lys  Ser Ala Asn Asn Thr  Pro Glu Asn
    1475                 1480                 1485


Ser Pro  Asn Phe Pro Asn Phe  Arg Val Ile Ala Thr  Lys Ser Ser
    1490                 1495                 1500


Glu Gln  Ser Arg Ser Val Asn  Ile Ala Ser Lys Leu  Ser Leu Gln
    1505                 1510                 1515


Glu Ser  Glu Ser Lys Arg Arg  Cys Arg Lys Arg Gln  Ser Pro Glu
    1520                 1525                 1530


Pro Ser  Pro Val Thr Leu Gly  Arg Arg Ser Ser Gly  Arg Gln Gly
    1535                 1540                 1545


Gly Val  His Glu Leu Ser Ala  Phe Glu Gln Leu Val  Val Glu Leu
    1550                 1555                 1560


Val Arg  His Asp Asp Ser Trp  Pro Phe Leu Lys Leu  Val Ser Lys
    1565                 1570                 1575


Ile Gln  Val Pro Asp Tyr Tyr  Asp Ile Ile Lys Lys  Pro Ile Ala
    1580                 1585                 1590


Leu Asn  Ile Ile Arg Glu Lys  Val Asn Lys Cys Glu  Tyr Lys Leu
    1595                 1600                 1605


Ala Ser  Glu Phe Ile Asp Asp  Ile Glu Leu Met Phe  Ser Asn Cys
    1610                 1615                 1620


Phe Glu  Tyr Asn Pro Arg Asn  Thr Ser Glu Ala Lys  Ala Gly Thr
    1625                 1630                 1635


Arg Leu  Gln Ala Phe Phe His  Ile Gln Ala Gln Lys  Leu Gly Leu
    1640                 1645                 1650


His Val  Thr Pro Ser Asn Val  Asp Gln Val Ser Thr  Pro Pro Ala
    1655                 1660                 1665
```

Ala Lys Lys Ser Arg Ile
    1670

<210> 2588
<211> 103
<212> PRT
<213> Homo sapiens

<400> 2588

Met Ala Gln Phe Val Arg Asn Leu Val Glu Lys Thr Pro Ala Leu Val
1   5   10   15

Asn Ala Ala Val Thr Tyr Ser Lys Pro Arg Leu Ala Thr Phe Trp Tyr
            20   25   30

Tyr Ala Lys Val Glu Leu Val Pro Pro Thr Pro Ala Glu Ile Pro Arg
        35   40   45

Ala Ile Gln Ser Leu Lys Lys Ile Ala Asn Ser Ala Gln Thr Gly Ser
    50   55   60

Phe Lys Gln Leu Thr Val Lys Glu Ala Val Leu Asn Gly Leu Val Ala
65   70   75   80

Thr Glu Val Leu Met Trp Phe Tyr Val Gly Glu Ile Ile Gly Lys Arg
                85   90   95

Gly Ile Ile Gly Tyr Asp Val
            100

<210> 2589
<211> 156
<212> PRT
<213> Homo sapiens

<400> 2589

Met Ser Gly Gly Leu Leu Lys Ala Leu Arg Ser Asp Ser Tyr Val Glu
1   5   10   15

Leu Ser Gln Tyr Arg Asp Gln His Phe Arg Gly Asp Asn Glu Glu Gln
            20   25   30

Glu Lys Leu Leu Lys Lys Ser Cys Thr Leu Tyr Val Gly Asn Leu Ser
        35   40   45

Phe Tyr Thr Thr Glu Glu Gln Ile Tyr Glu Leu Phe Ser Lys Ser Gly
    50   55   60

Asp Ile Lys Lys Ile Ile Met Gly Leu Asp Lys Met Lys Lys Thr Ala
65   70   75   80

Cys Gly Phe Cys Phe Val Glu Tyr Tyr Ser Arg Ala Asp Ala Glu Asn
                85   90   95

Ala Met Arg Tyr Ile Asn Gly Thr Arg Leu Asp Asp Arg Ile Ile Arg
            100   105   110

Thr Asp Trp Asp Ala Gly Phe Lys Glu Gly Arg Gln Tyr Gly Arg Gly
        115   120   125

Arg Ser Gly Gly Gln Val Arg Asp Glu Tyr Arg Gln Asp Tyr Asp Ala
    130   135   140

Gly Arg Gly Gly Tyr Gly Lys Leu Ala Gln Asn Gln
145   150   155

<210>   2590
<211>   436
<212>   PRT
<213>   Homo sapiens

<400>   2590

Met Asp Ser Val Ala Phe Glu Asp Val Ala Val Asn Phe Thr Gln Glu
1   5   10   15

Glu Trp Ala Leu Leu Ser Pro Ser Gln Lys Asn Leu Tyr Arg Asp Val
            20   25   ·   30

Thr Leu Glu Thr Phe Arg Asn Leu Ala Ser Val Gly Ile Gln Trp Lys
            35   40   45

Asp Gln Asp Ile Glu Asn Leu Tyr Gln Asn Leu Gly Ile Lys Leu Arg
    50   55   60

Ser Leu Val Glu Arg Leu Cys Gly Arg Lys Glu Gly Asn Glu His Arg
65   70   75   80

Glu Thr Phe Ser Gln Ile Pro Asp Cys His Leu Asn Lys Lys Ser Gln
                85   90   95

Thr Gly Val Lys Pro Cys Lys Cys Ser Val Cys Gly Lys Val Phe Leu
            100   105   110

```
Arg His Ser Phe Leu Asp Arg His Met Arg Ala His Ala Gly His Lys
        115                 120             125

Arg Ser Glu Cys Gly Gly Glu Trp Arg Glu Thr Pro Arg Lys Gln Lys
        130                 135             140

Gln His Gly Lys Ala Ser Ile Ser Pro Ser Ser Gly Ala Arg Arg Thr
145                 150                 155                 160

Val Thr Pro Thr Arg Lys Arg Pro Tyr Glu Cys Lys Val Cys Gly Lys
                165                 170                 175

Ala Phe Asn Ser Pro Asn Leu Phe Gln Ile His Gln Arg Thr His Thr
            180                 185                 190

Gly Lys Arg Ser Tyr Lys Cys Arg Glu Ile Val Arg Ala Phe Thr Val
        195                 200                 205

Ser Ser Phe Phe Arg Lys His Gly Lys Met His Thr Gly Glu Lys Arg
210                 215                 220

Tyr Glu Cys Lys Tyr Cys Gly Lys Pro Ile Asp Tyr Pro Ser Leu Phe
225                 230                 235                 240

Gln Ile His Val Arg Thr His Thr Gly Glu Lys Pro Tyr Lys Cys Lys
            245                 250                 255

Gln Cys Gly Lys Ala Phe Ile Ser Ala Gly Tyr Leu Arg Thr His Glu
        260                 265                 270

Ile Arg Ser His Ala Leu Glu Lys Ser His Gln Cys Gln Glu Cys Gly
        275                 280                 285

Lys Lys Leu Ser Cys Ser Ser Ser Leu His Arg His Glu Arg Thr His
    290                 295                 300

Ser Gly Gly Lys Leu Tyr Glu Cys Gln Lys Cys Ala Lys Val Phe Arg
305                 310                 315                 320

Cys Pro Thr Ser Leu Gln Ala His Glu Arg Ala His Thr Gly Glu Arg
            325                 330                 335

Pro Tyr Glu Cys Asn Lys Cys Gly Lys Thr Phe Asn Tyr Pro Ser Cys
        340                 345                 350

Phe Arg Arg His Lys Lys Thr His Ser Gly Glu Lys Pro Tyr Glu Cys
```

                    355   360   365

      Thr Arg Cys Gly Lys Ala Phe Gly Trp Cys Ser Ser Leu Arg Arg His
          370   375   380

      Glu Met Thr His Thr Gly Glu Lys Pro Phe Asp Cys Lys Gln Cys Gly
      385   390   395   400

      Lys Val Phe Thr Phe Ser Asn Tyr Leu Arg Leu His Glu Arg Thr His
                      405   410   415

      Leu Ala Gly Arg Ser Gln Cys Phe Gly Arg Arg Gln Gly Asp His Leu
                  420   425   430

      Ser Pro Gly Val
              435

      <210>   2591
      <211>   92
      <212>   PRT
      <213>   Homo sapiens

      <400>   2591

      Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
      1   5   10   15

      Leu Cys Asn Gln Phe Ser Ala Ser Leu Ala Ala Asp Thr Pro Thr Ala
                  20   25   30

      Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala
                  35   40   45

      Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe
          50   55   60

      Leu Thr Lys Arg Ser Arg Gln Val Cys Ala Asp Pro Ser Glu Glu Trp
      65   70   75   80

      Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                      85   90

      <210>   2592
      <211>   271
      <212>   PRT
      <213>   Homo sapiens

      <400>   2592

```
Met Glu Ala Leu Pro Leu Leu Ala Ala Thr Thr Pro Asp His Gly Arg
1                5                10              15

His Arg Arg Leu Leu Leu Leu Pro Leu Leu Leu Phe Leu Leu Pro Ala
            20              25              30

Gly Ala Val Gln Gly Trp Glu Thr Glu Glu Arg Pro Arg Thr Arg Glu
        35              40              45

Glu Glu Cys His Phe Tyr Ala Gly Gly Gln Val Tyr Pro Gly Glu Ala
    50              55              60

Ser Arg Val Ser Val Ala Asp His Ser Leu His Leu Ser Lys Ala Lys
65              70              75              80

Ile Ser Lys Pro Ala Pro Tyr Trp Glu Gly Thr Ala Val Ile Asp Gly
            85              90              95

Glu Phe Lys Glu Leu Lys Leu Thr Asp Tyr Arg Gly Lys Tyr Leu Val
            100             105             110

Phe Phe Phe Tyr Pro Leu Asp Phe Thr Phe Val Cys Pro Thr Glu Ile
        115             120             125

Ile Ala Phe Gly Asp Arg Leu Glu Glu Phe Arg Ser Ile Asn Thr Glu
    130             135             140

Val Val Ala Cys Ser Val Asp Ser Gln Phe Thr His Leu Ala Trp Ile
145             150             155             160

Asn Thr Pro Arg Arg Gln Gly Gly Leu Gly Pro Ile Arg Ile Pro Leu
            165             170             175

Leu Ser Asp Leu Thr His Gln Ile Ser Lys Asp Tyr Gly Val Tyr Leu
            180             185             190

Glu Asp Ser Gly His Thr Leu Arg Gly Leu Phe Ile Ile Asp Asp Lys
        195             200             205

Gly Ile Leu Arg Gln Ile Thr Leu Asn Asp Leu Pro Val Gly Arg Ser
    210             215             220

Val Asp Glu Thr Leu Arg Leu Val Gln Ala Phe Gln Tyr Thr Asp Lys
225             230             235             240

His Gly Glu Val Cys Pro Ala Gly Trp Lys Pro Gly Ser Glu Thr Ile
```

<div align="center">245   250   255</div>

Ile Pro Asp Pro Ala Gly Lys Leu Lys Tyr Phe Asp Lys Leu Asn
            260   265   270,

<210> 2593
<211> 659
<212> PRT
<213> Homo sapiens

<400> 2593

Met Ala Ala Val Ile Leu Glu Ser Ile Phe Leu Lys Arg Ser Gln Gln
1   5   10   15

Lys Lys Lys Thr Ser Pro Leu Asn Phe Lys Lys Arg Leu Phe Leu Leu
            20   25   30

Thr Val His Lys Leu Ser Tyr Tyr Glu Tyr Asp Phe Glu Arg Gly Arg
        35   40   45

Arg Gly Ser Lys Lys Gly Ser Ile Asp Val Glu Lys Ile Thr Cys Val
        50   55   60

Glu Thr Val Val Pro Glu Lys Asn Pro Pro Glu Arg Gln Ile Pro
65   70   75   80

Arg Arg Gly Glu Glu Ser Ser Glu Met Glu Gln Ile Ser Ile Ile Glu
                85   90   95

Arg Phe Pro Tyr Pro Phe Gln Val Val Tyr Asp Glu Gly Pro Leu Tyr
            100   105   110

Val Phe Ser Pro Thr Glu Glu Leu Arg Lys Arg Trp Ile His Gln Leu
        115   120   125

Lys Asn Val Ile Arg Tyr Asn Ser Asp Leu Val Gln Lys Tyr His Pro
        130   135   140

Cys Phe Trp Ile Asp Gly Gln Tyr Leu Cys Cys Ser Gln Thr Ala Lys
145   150   155   160

Asn Ala Met Gly Cys Gln Ile Leu Glu Asn Arg Asn Gly Ser Leu Lys
                165   170   175

Pro Gly Ser Ser His Arg Lys Thr Lys Lys Pro Leu Pro Pro Thr Pro
            180   185   190

<div align="center">1019</div>

```
Glu Glu Asp Gln Ile Leu Lys Lys Pro Leu Pro Pro Glu Pro Ala Ala
        195             200         205


Ala Pro Val Ser Thr Ser Glu Leu Lys Lys Val Val Ala Leu Tyr Asp
    210             215             220


Tyr Met Pro Met Asn Ala Asn Asp Leu Gln Leu Arg Lys Gly Asp Glu
225             230             235             240


Tyr Phe Ile Leu Glu Glu Ser Asn Leu Pro Trp Trp Arg Ala Arg Asp
            245             250             255


Lys Asn Gly Gln Glu Gly Tyr Ile Pro Ser Asn Tyr Val Thr Glu Ala
        260             265             270


Glu Asp Ser Ile Glu Met Tyr Glu Trp Tyr Ser Lys His Met Thr Arg
        275             280             285


Ser Gln Ala Glu Gln Leu Leu Lys Gln Glu Gly Lys Glu Gly Gly Phe
    290             295             300


Ile Val Arg Asp Ser Ser Lys Ala Gly Lys Tyr Thr Val Ser Val Phe
305             310             315             320


Ala Lys Ser Thr Gly Asp Pro Gln Gly Val Ile Arg His Tyr Val Val
            325             330             335


Cys Ser Thr Pro Gln Ser Gln Tyr Tyr Leu Ala Glu Lys His Leu Phe
            340             345             350


Ser Thr Ile Pro Glu Leu Ile Asn Tyr His Gln His Asn Ser Ala Gly
        355             360             365


Leu Ile Ser Arg Leu Lys Tyr Pro Val Ser Gln Gln Asn Lys Asn Ala
        370             375             380


Pro Ser Thr Ala Gly Leu Gly Tyr Gly Ser Trp Glu Ile Asp Pro Lys
385             390             395             400


Asp Leu Thr Phe Leu Lys Glu Leu Gly Thr Gly Gln Phe Gly Val Val
            405             410             415


Lys Tyr Gly Lys Trp Arg Gly Gln Tyr Asp Val Ala Ile Lys Met Ile
        420             425             430
```

```
Lys Glu Gly Ser Met Ser Glu Asp Glu Phe Ile Glu Glu Ala Lys Val
        435             440                 445

Met Met Asn Leu Ser His Glu Lys Leu Val Gln Leu Tyr Gly Val Cys
    450             455                 460

Thr Lys Gln Arg Pro Ile Phe Ile Ile Thr Glu Tyr Met Ala Asn Gly
465             470                 475                 480

Cys Leu Leu Asn Tyr Leu Arg Glu Met Arg His Arg Phe Gln Thr Gln
            485             490                 495

Gln Leu Leu Glu Met Cys Lys Asp Val Cys Glu Ala Met Glu Tyr Leu
        500             505                 510

Glu Ser Lys Gln Phe Leu His Arg Asp Leu Ala Ala Arg Asn Cys Leu
        515             520                 525

Val Asn Asp Gln Gly Val Val Lys Val Ser Asp Phe Gly Leu Ser Arg
    530             535                 540

Tyr Val Leu Asp Asp Glu Tyr Thr Ser Ser Val Gly Ser Lys Phe Pro
545             550                 555                 560

Val Arg Trp Ser Pro Pro Glu Val Leu Met Tyr Ser Lys Phe Ser Ser
            565             570                 575

Lys Ser Asp Ile Trp Ala Phe Gly Val Leu Met Trp Glu Ile Tyr Ser
            580             585                 590

Leu Gly Lys Met Pro Tyr Glu Arg Phe Thr Asn Ser Glu Thr Ala Glu
        595             600                 605

His Ile Ala Gln Gly Leu Arg Leu Tyr Arg Pro His Leu Ala Ser Glu
    610             615                 620

Lys Val Tyr Thr Ile Met Tyr Ser Cys Trp His Glu Lys Ala Asp Glu
625             630                 635                 640

Arg Pro Thr Phe Lys Ile Leu Leu Ser Asn Ile Leu Asp Val Met Asp
            645             650                 655

Glu Glu Ser
```

<210> 2594

<211>   417
<212>   PRT
<213>   Homo sapiens

<400>   2594

```
Met Ser Leu Ser Asn Lys Leu Thr Leu Asp Lys Leu Asp Val Lys Gly
1               5                   10                  15

Lys Arg Val Val Met Arg Val Asp Phe Asn Val Pro Met Lys Asn Asn
            20                  25                  30

Gln Ile Thr Asn Asn Gln Arg Ile Lys Ala Ala Val Pro Ser Ile Lys
            35                  40                  45

Phe Cys Leu Asp Asn Gly Ala Lys Ser Val Val Leu Met Ser His Leu
    50                  55                  60

Gly Arg Pro Asp Gly Val Pro Met Pro Asp Lys Tyr Ser Leu Glu Pro
65                  70                  75                  80

Val Ala Val Glu Leu Lys Ser Leu Leu Gly Lys Asp Val Leu Phe Leu
                85                  90                  95

Lys Asp Cys Val Gly Pro Glu Val Glu Lys Ala Cys Ala Asn Pro Ala
            100                 105                 110

Ala Gly Ser Val Ile Leu Leu Glu Asn Leu Arg Phe His Val Glu Glu
            115                 120                 125

Glu Gly Lys Gly Lys Asp Ala Ser Gly Asn Lys Val Lys Ala Glu Pro
    130                 135                 140

Ala Lys Ile Glu Ala Phe Arg Ala Ser Leu Ser Lys Leu Gly Asp Val
145                 150                 155                 160

Tyr Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ser Ser Met
                165                 170                 175

Val Gly Val Asn Leu Pro Gln Lys Ala Gly Gly Phe Leu Met Lys Lys
            180                 185                 190

Glu Leu Asn Tyr Phe Ala Lys Ala Leu Glu Ser Pro Glu Arg Pro Phe
    195                 200                 205

Leu Ala Ile Leu Gly Gly Ala Lys Val Ala Asp Lys Ile Gln Leu Ile
    210                 215                 220
```

Asn Asn Met Leu Asp Lys Val Asn Glu Met Ile Ile Gly Gly Gly Met
225   230   235   240

Ala Phe Thr Phe Leu Lys Val Leu Asn Asn Met Glu Ile Gly Thr Ser
                245   250   255

Leu Phe Asp Glu Glu Gly Ala Lys Ile Val Lys Asp Leu Met Ser Lys
            260   265   270

Ala Glu Lys Asn Gly Val Lys Ile Thr Leu Pro Val Asp Phe Val Thr
        275   280   285

Ala Asp Lys Phe Asp Glu Asn Ala Lys Thr Gly Gln Ala Thr Val Ala
    290   295   ·   300

Ser Gly Ile Pro Ala Gly Trp Met Gly Leu Asp Cys Gly Pro Glu Ser
305   310   315   320

Ser Lys Lys Tyr Ala Glu Ala Val Thr Arg Ala Lys Gln Ile Val Trp
            325   330   335

Asn Gly Pro Val Gly Val Phe Glu Trp Glu Ala Phe Ala Arg Gly Thr
            340   345   350

Lys Ala Leu Met Asp Glu Val Val Lys Ala Thr Ser Arg Gly Cys Ile
        355   360   365

Thr Ile Ile Gly Gly Gly Asp Thr Ala Thr Cys Cys Ala Lys Trp Asn
    370   375   380

Thr Glu Asp Lys Val Ser His Val Ser Thr Gly Gly Gly Ala Ser Leu
385   390   395   400

Glu Leu Leu Glu Gly Lys Val Leu Pro Gly Val Asp Ala Leu Ser Asn
            405   410   415

Ile

<210> 2595
<211> 468
<212> PRT
<213> Homo sapiens

<400> 2595

Met Ala Pro Pro Pro Ala Arg Val His Leu Gly Ala Phe Leu Ala Val

```
1                    5                      10                    15


      Thr Pro Asn Pro Gly Ser Ala Ala Ser Gly Thr Glu Ala Ala Ala Ala
              20                  25                  30


      Thr Pro Ser Lys Val Trp Gly Ser Ser Ala Gly Arg Ile Glu Pro Arg
              35                  40                  45


      Gly Gly Gly Arg Gly Ala Leu Pro Thr Ser Met Gly Gln His Gly Pro
              50                  55                  60


      Ser Ala Arg Ala Arg Ala Gly Arg Ala Pro Gly Pro Arg Pro Ala Arg
      65                  70                  75                  80


      Glu Ala Ser Pro Arg Leu Arg Val His Lys Thr Phe Lys Phe Val Val
                      85                  90                  95


      Val Gly Val Leu Leu Gln Val Val Pro Ser Ser Ala Ala Thr Ile Lys
                      100                 105                 110


      Leu His Asp Gln Ser Ile Gly Thr Gln Gln Trp Glu His Ser Pro Leu
                      115                 120                 125


      Gly Glu Leu Cys Pro Pro Gly Ser His Arg Ser Glu His Pro Gly Ala
              130                 135                 140


      Cys Asn Arg Cys Thr Glu Gly Val Gly Tyr Thr Asn Ala Ser Asn Asn
      145                 150                 155                 160


      Leu Phe Ala Cys Leu Pro Cys Thr Ala Cys Lys Ser Asp Glu Glu Glu
                      165                 170                 175


      Arg Ser Pro Cys Thr Thr Thr Arg Asn Thr Ala Cys Gln Cys Lys Pro
                      180                 185                 190


      Gly Thr Phe Arg Asn Asp Asn Ser Ala Glu Met Cys Arg Lys Cys Ser
              195                 200                 205


      Arg Gly Cys Pro Arg Gly Met Val Lys Val Lys Asp Cys Thr Pro Trp
      210                 215                 220


      Ser Asp Ile Glu Cys Val His Lys Glu Ser Gly Asn Gly His Asn Ile
      225                 230                 235                 240


      Trp Val Ile Leu Val Val Thr Leu Val Val Pro Leu Leu Leu Val Ala
                      245                 250                 255
```

```
Val Leu Ile Val Cys Cys Cys Ile Gly Ser Gly Cys Gly Gly Asp Pro
          260             265             270

Lys Cys Met Asp Arg Val Cys Phe Trp Arg Leu Gly Leu Leu Arg Gly
      275             280             285

Pro Gly Ala Glu Asp Asn Ala His Asn Glu Ile Leu Ser Asn Ala Asp
      290             295             300

Ser Leu Ser Thr Phe Val Ser Glu Gln Gln Met Glu Ser Gln Glu Pro
305             310             315             320

Ala Asp Leu Thr Gly Val Thr Val Gln Ser Pro Gly Glu Ala Gln Cys
              325             330             335

Leu Leu Gly Pro Ala Glu Ala Glu Gly Ser Gln Arg Arg Arg Leu Leu
          340             345             350

Val Pro Ala Asn Gly Ala Asp Pro Thr Glu Thr Leu Met Leu Phe Phe
      355             360             365

Asp Lys Phe Ala Asn Ile Val Pro Phe Asp Ser Trp Asp Gln Leu Met
    370             375             380

Arg Gln Leu Asp Leu Thr Lys Asn Glu Ile Asp Val Val Arg Ala Gly
385             390             395             400

Thr Ala Gly Pro Gly Asp Ala Leu Tyr Ala Met Leu Met Lys Trp Val
              405             410             415

Asn Lys Thr Gly Arg Asn Ala Ser Ile His Thr Leu Leu Asp Ala Leu
          420             425             430

Glu Arg Met Glu Glu Arg His Ala Lys Glu Lys Ile Gln Asp Leu Leu
      435             440             445

Val Asp Ser Gly Lys Phe Ile Tyr Leu Glu Asp Gly Thr Gly Ser Ala
    450             455             460

Val Ser Leu Glu
465


<210>  2596
<211>  185
<212>  PRT
```

<213>   Homo sapiens

<400>   2596

Met Lys Leu Val Ser Val Ala Leu Met Tyr Leu Gly Ser Leu Ala Phe
1   5   10   15

Leu Gly Ala Asp Thr Ala Arg Leu Asp Val Ala Ser Glu Phe Arg Lys
            20   25   30

Lys Trp Asn Lys Trp Ala Leu Ser Arg Gly Lys Arg Glu Leu Arg Met
        35   40   45

Ser Ser Ser Tyr Pro Thr Gly Leu Ala Asp Val Lys Ala Gly Pro Ala
    50   55   60

Gln Thr Leu Ile Arg Pro Gln Asp Met Lys Gly Ala Ser Arg Ser Pro
65   70   75   80

Glu Asp Ser Ser Pro Asp Ala Ala Arg Ile Arg Val Lys Arg Tyr Arg
            85   90   95

Gln Ser Met Asn Asn Phe Gln Gly Leu Arg Ser Phe Gly Cys Arg Phe
            100   105   110

Gly Thr Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln Phe Thr
        115   120   125

Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys Ile Ser Pro Gln
    130   135   140

Gly Tyr Gly Arg Arg Arg Arg Ser Leu Pro Glu Ala Gly Pro Gly
145   150   155   160

Arg Thr Leu Val Ser Ser Lys Pro Gln Ala His Gly Ala Pro Ala Pro
            165   170   175

Pro Ser Gly Ser Ala Pro His Phe Leu
            180   185

<210>   2597
<211>   851
<212>   PRT
<213>   Homo sapiens

<400>   2597

Met Ser Ser Lys Gln Glu Ile Met Ser Asp Gln Arg Phe Arg Arg Val
1   5   10   15

```
Ala Lys Asp Pro Arg Phe Trp Glu Met Pro Glu Lys Asp Arg Lys Val
            20                  25              30

Lys Ile Asp Lys Arg Phe Arg Ala Met Phe His Asp Lys Lys Phe Lys
            35              40              45

Leu Asn Tyr Ala Val Asp Lys Arg Gly Arg Pro Ile Ser His Ser Thr
    50              55              60

Thr Glu Asp Leu Lys Arg Phe Tyr Asp Leu Ser Asp Ser Asp Ser Asn
65                  70              75                  80

Leu Ser Gly Glu Asp Ser Lys Ala Leu Ser Gln Lys Lys Ile Lys Lys
                85              90              95

Lys Lys Thr Gln Thr Lys Lys Glu Ile Asp Ser Lys Asn Leu Val Glu
            100             105             110

Lys Lys Lys Glu Thr Lys Lys Ala Asn His Lys Gly Ser Glu Asn Lys
            115             120             125

Thr Asp Leu Asp Asn Ser Ile Gly Ile Lys Lys Met Lys Thr Ser Cys
    130             135             140

Lys Phe Lys Ile Asp Ser Asn Ile Ser Pro Lys Lys Asp Ser Lys Glu
145             150             155             160

Phe Thr Gln Lys Asn Lys Lys Glu Lys Lys Asn Ile Val Gln His Thr
            165             170             175

Thr Asp Ser Ser Leu Glu Glu Lys Gln Arg Thr Leu Asp Ser Gly Thr
            180             185             190

Ser Glu Ile Val Lys Ser Pro Arg Ile Glu Cys Ser Lys Thr Arg Arg
    195             200             205

Glu Met Gln Ser Val Val Gln Leu Ile Met Thr Arg Asp Ser Asp Gly
    210             215             220

Tyr Glu Asn Ser Thr Asp Gly Glu Met Cys Asp Lys Asp Ala Leu Glu
225             230             235             240

Glu Asp Ser Glu Ser Val Ser Glu Ile Gly Ser Asp Glu Glu Ser Glu
                245             250             255
```

```
Asn Glu Ile Thr Ser Val Gly Arg Ala Ser Gly Asp Asp Asp Gly Ser
            260             265             270

Glu Asp Asp Glu Glu Glu Asp Glu Asp Glu Glu Glu Asp Glu Asp Glu
        275             280             285

Asp Ser Glu Asp Asp Asp Lys Ser Asp Ser Gly Pro Asp Leu Ala Arg
    290             295             300

Gly Lys Gly Asn Ile Glu Thr Ser Ser Glu Asp Glu Asp Thr Ala
305             310             315             320

Asp Leu Phe Pro Glu Glu Ser Gly Phe Glu His Ala Trp Arg Glu Leu
            325             330             335

Asp Lys Asp Ala Pro Arg Ala Asp Glu Ile Thr Arg Arg Leu Ala Val
            340             345             350

Cys Asn Met Asp Trp Asp Arg Leu Lys Ala Lys Asp Leu Leu Ala Leu
            355             360             365

Phe Asn Ser Phe Lys Pro Lys Gly Gly Val Ile Phe Ser Val Lys Ile
    370             375             380

Tyr Pro Ser Glu Phe Gly Lys Glu Arg Met Lys Glu Glu Gln Val Gln
385             390             395             400

Gly Pro Val Glu Leu Leu Ser Ile Pro Glu Asp Ala Pro Glu Lys Asp
            405             410             415

Trp Thr Ser Arg Glu Lys Leu Arg Asp Tyr Gln Phe Lys Arg Leu Lys
            420             425             430

Tyr Tyr Tyr Ala Val Val Asp Cys Asp Ser Pro Glu Thr Ala Ser Lys
        435             440             445

Ile Tyr Glu Asp Cys Asp Gly Leu Glu Phe Glu Ser Ser Cys Ser Phe
    450             455             460

Ile Asp Leu Arg Phe Ile Pro Asp Asp Ile Thr Phe Asp Asp Glu Pro
465             470             475             480

Lys Asp Val Ala Ser Glu Val Asn Leu Thr Ala Tyr Lys Pro Lys Tyr
            485             490             495
```

Phe Thr Ser Ala Ala Met Gly Thr Ser Thr Val Glu Ile Thr Trp Asp
        500   505   510

Glu Thr Asp His Glu Arg Ile Thr Met Leu Asn Arg Lys Phe Lys Lys
        515   520   525

Glu Glu Leu Leu Asp Met Asp Phe Gln Ala Tyr Leu Ala Ser Ser Ser
        530   535   540

Glu Asp Glu Glu Glu Ile Glu Glu Glu Leu Gln Gly Asp Asp Gly Val
545   550   555   560

Asn Val Glu Glu Asp Gly Lys Thr Lys Lys Ser Gln Lys Asp Asp Glu
            565   570   575

Glu Gln Ile Ala Lys Tyr Arg Gln Leu Leu Gln Val Ile Gln Glu Lys
            580   585   590

Glu Lys Lys Gly Lys Glu Asn Asp Met Glu Met Glu Ile Lys Trp Val
        595   600   605

Pro Gly Leu Lys Glu Ser Ala Glu Glu Met Val Lys Asn Lys Leu Glu
    610   615   620

Gly Lys Asp Lys Leu Thr Pro Trp Glu Gln Phe Leu Glu Lys Lys Lys
625   630   635   640

Glu Lys Lys Arg Leu Lys Arg Lys Gln Lys Ala Leu Ala Glu Glu Ala
            645   650   655

Ser Glu Glu Glu Leu Pro Ser Asp Val Asp Leu Asn Asp Pro Tyr Phe
            660   665   670

Ala Glu Glu Val Lys Gln Ile Gly Ile Asn Lys Lys Ser Val Lys Ser
        675   680   685

Ala Lys Asp Gly Thr Ser Pro Glu Glu Glu Ile Glu Ile Glu Arg Gln
        690   695   700

Lys Ala Glu Met Ala Leu Leu Met Met Asp Glu Asp Glu Asp Ser Lys
705   710   715   720

Lys His Phe Asn Tyr Asn Lys Ile Val Glu His Gln Asn Leu Ser Lys
            725   730   735

Lys Lys Lys Lys Gln Leu Met Lys Lys Lys Glu Leu Ile Glu Asp Asp

```
                 740                      745                     750
```

Phe Glu Val Asn Val Asn Asp Ala Arg Phe Gln Ala Met Tyr Thr Ser
        755   760   765

His Leu Phe Asn Leu Asp Pro Ser Asp Pro Asn Phe Lys Lys Thr Lys
    770   775   780

Ala Met Glu Lys Ile Leu Glu Glu Lys Ala Arg Gln Arg Glu Arg Lys
785   790   795   800

Glu Gln Glu Leu Thr Gln Ala Ile Lys Lys Glu Ser Glu Ile Glu
                805   810   815

Lys Glu Ser Gln Arg Lys Ser Ile Asp Pro Ala Leu Ser Met Leu Ile
        820   825   830

Lys Ser Ile Lys Thr Lys Thr Glu Gln Phe Gln Ala Arg Lys Lys Gln
        835   840   845

Lys Val Lys
    850

<210> 2598
<211> 244
<212> PRT
<213> Homo sapiens

<400> 2598

Met Val Tyr Lys Thr Leu Phe Ala Leu Cys Ile Leu Thr Ala Gly Trp
1   5   10   15

Arg Val Gln Ser Leu Pro Thr Ser Ala Pro Leu Ser Val Ser Leu Pro
            20   25   30

Thr Asn Ile Val Pro Pro Thr Thr Ile Trp Thr Ser Ser Pro Gln Asn
        35   40   45

Thr Asp Ala Asp Thr Ala Ser Pro Ser Asn Gly Thr His Asn Asn Ser
    50   55   60

Val Leu Pro Val Thr Ala Ser Ala Pro Thr Ser Leu Leu Pro Lys Asn
65   70   75   80

Ile Ser Ile Glu Ser Arg Glu Glu Glu Ile Thr Ser Pro Gly Ser Asn
                85   90   95

                                  1030

Trp Glu Gly Thr Asn Thr Asp Pro Ser Pro Ser Gly Phe Ser Ser Thr
            100   105   110

Ser Gly Gly Val His Leu Thr Thr Thr Leu Glu Glu His Ser Leu Gly
        115   120   125

Thr Pro Glu Ala Gly Val Ala Ala Thr Leu Ser Gln Ser Ala Ala Glu
    130   135   140

Pro Pro Thr Leu Ile Ser Pro Gln Ala Pro Ala Ser Ser Pro Ser Ser
145   150   155   160

Leu Ser Thr Ser Pro Pro Glu Val Phe Ser Ala Ser Val Thr Thr Asn
                165   170   175

His Ser Ser Thr Val Thr Ser Thr Gln Pro Thr Gly Ala Pro Thr Ala
            180   185   190

Pro Glu Ser Pro Thr Glu Glu Ser Ser Ser Asp His Thr Pro Thr Ser
        195   200   205

His Ala Thr Ala Glu Pro Val Pro Gln Glu Lys Thr Pro Pro Thr Thr
210   215   220

Val Ser Gly Lys Val Met Cys Glu Leu Ile Asp Met Glu Thr Pro Pro
225   230   235   240

Pro Phe Pro Gly

<210> 2599
<211> 395
<212> PRT
<213> Homo sapiens

<400> 2599

Met Pro Gly Arg Ser Cys Val Ala Leu Val Leu Leu Ala Ala Ala Val
1   5   10   15

Ser Cys Ala Val Ala Gln His Ala Pro Pro Trp Thr Glu Asp Cys Arg
            20   25   30

Lys Ser Thr Tyr Pro Pro Ser Gly Pro Thr Tyr Arg Gly Ala Val Pro
        35   40   45

Trp Tyr Thr Ile Asn Leu Asp Leu Pro Pro Tyr Lys Arg Trp His Glu

```
        50                      55                      60
```

Leu Met Leu Asp Lys Ala Pro Met Leu Lys Val Ile Val Asn Ser Leu
65   .   70   75   80

Lys Asn Met Ile Asn Thr Phe Val Pro Ser Gly Lys Val Met Gln Val
                    85   90   95

Val Asp Glu Lys Leu Pro Gly Leu Leu Gly Asn Phe Pro Gly Pro Phe
            100   105   110

Glu Glu Glu Met Lys Gly Ile Ala Ala Val Thr Asp Ile Pro Leu Gly
        115   120   125

Glu Ile Ile Ser Phe Asn Ile Phe Tyr Glu Leu Phe Thr Ile Cys Thr
        130   135   140

Ser Ile Val Ala Glu Asp Lys Lys Gly His Leu Ile His Gly Arg Asn
145   150   155   160

Met Asp Phe Gly Val Phe Leu Gly Trp Asn Ile Asn Asn Asp Thr Trp .
            165   170   175

Val Ile Thr Glu Gln Leu Lys Pro Leu Thr Val Asn Leu Asp Phe Gln
        180   185   190

Arg Asn Asn Lys Thr Val Phe Lys Ala Ser Ser Phe Ala Gly Tyr Val
        195   200   205

Gly Met Leu Thr Gly Phe Lys Pro Gly Leu Phe Ser Leu Thr Leu Asn
    210   215   220

Glu Arg Phe Ser Ile Asn Gly Gly Tyr Leu Gly Ile Leu Glu Trp Ile
225   230   235   240

Leu Gly Lys Lys Asp Ala Met Trp Ile Gly Phe Leu Thr Arg Thr Val
            245   250   255

Leu Glu Asn Ser Thr Ser Tyr Glu Glu Ala Lys Asn Leu Leu Thr Lys
        260   265   270

Thr Lys Ile Leu Ala Pro Ala Tyr Phe Ile Leu Gly Gly Asn Gln Ser
        275   280   285

Gly Glu Gly Cys Val Ile Thr Arg Asp Arg Lys Glu Ser Leu Asp Val
    290   295   300

```
Tyr Glu Leu Asp Ala Lys Gln Gly Arg Trp Tyr Val Val Gln Thr Asn
305             310             315             320

Tyr Asp Arg Trp Lys His Pro Phe Phe Leu Asp Asp Arg Arg Thr Pro
            325             330             335

Ala Lys Met Cys Leu Asn Arg Thr Ser Gln Glu Asn Ile Ser Phe Glu
        340             345             350

Thr Met Tyr Asp Val Leu Ser Thr Lys Pro Val Leu Asn Lys Leu Thr
        355             360             365

Val Tyr Thr Thr Leu Ile Asp Val Thr Lys Gly Gln Phe Glu Thr Tyr
370             375             380

Leu Arg Asp Cys Pro Asp Pro Cys Ile Gly Trp
385             390             395
```

```
<210>   2600
<211>   282
<212>   PRT
<213>   Homo sapiens

<400>   2600
```

```
Met Ser Leu Leu Ala Thr Leu Gly Leu Glu Leu Asp Arg Ala Leu Leu
1               5               10              15

Pro Ala Ser Gly Leu Gly Trp Leu Val Asp Tyr Gly Lys Leu Pro Pro
            20              25              30

Ala Pro Ala Pro Leu Ala Pro Tyr Glu Val Leu Gly Gly Ala Leu Glu
        35              40              45

Gly Gly Leu Pro Val Gly Gly Glu Pro Leu Ala Gly Asp Gly Phe Ser
    50              55              60

Asp Trp Met Thr Glu Arg Val Asp Phe Thr Ala Leu Leu Pro Leu Glu
65              70              75              80

Pro Pro Leu Pro Pro Gly Thr Leu Pro Gln Pro Ser Pro Thr Pro Pro
            85              90              95

Asp Leu Glu Ala Met Ala Ser Leu Leu Lys Lys Glu Leu Glu Gln Met
        100             105             110
```

```
Glu Asp Phe Phe Leu Asp Ala Pro Pro Leu Pro Pro Pro Ser Pro Pro
    115             120             125
```

```
Pro Leu Pro Pro Pro Pro Leu Pro Pro Ala Pro Ser Leu Pro Leu Ser
    130             135             140
```

```
Leu Pro Ser Phe Asp Leu Pro Gln Pro Pro Val Leu Asp Thr Leu Asp
145             150             155             160
```

```
Leu Leu Ala Ile Tyr Cys Arg Asn Glu Ala Gly Gln Glu Glu Val Gly
            165             170             175
```

```
Met Pro Pro Leu Pro Pro Pro Gln Gln Pro Pro Pro Pro Ser Pro Pro
        180             185             190
```

```
Gln Pro Ser Arg Leu Ala Pro Tyr Pro His Pro Ala Thr Thr Arg Gly
    195             200             205
```

```
Asp Arg Lys Gln Lys Lys Arg Asp Gln Asn Lys Ser Ala Ala Leu Arg
210             215             220
```

```
Tyr Arg Gln Arg Lys Arg Ala Glu Gly Glu Ala Leu Glu Gly Glu Cys
225             230             235             240
```

```
Gln Gly Leu Glu Ala Arg Asn Arg Glu Leu Lys Glu Arg Ala Glu Ser
            245             250             255
```

```
Val Glu Arg Glu Ile Gln Tyr Val Lys Asp Leu Leu Ile Glu Val Tyr
        260             265             270
```

```
Lys Ala Arg Ser Gln Arg Thr Arg Ser Cys
    275             280
```

```
<210>  2601
<211>  23
<212>  PRT
<213>  Homo sapiens

<400>  2601

Met Glu Thr Ser Glu Gly Pro Gly Leu Glu Ser Thr Gly Ser Tyr Leu
1               5               10              15

Gly Ile Gln Gln Arg Ser Pro
            20


<210>  2602
<211>  491
```

<212> PRT
<213> Homo sapiens

<400> 2602

Met Cys Asn Thr Asn Met Ser Val Pro Thr Asp Gly Ala Val Thr Thr
1   5   10   15

Ser Gln Ile Pro Ala Ser Glu Gln Glu Thr Leu Val Arg Pro Lys Pro
                20   25   30

Leu Leu Leu Lys Leu Leu Lys Ser Val Gly Ala Gln Lys Asp Thr Tyr
            35   40   45

Thr Met Lys Glu Val Leu Phe Tyr Leu Gly Gln Tyr Ile Met Thr Lys
    50   55   60

Arg Leu Tyr Asp Glu Lys Gln Gln His Ile Val Tyr Cys Ser Asn Asp
65   70   75   80

Leu Leu Gly Asp Leu Phe Gly Val Pro Ser Phe Ser Val Lys Glu His
                85   90   95

Arg Lys Ile Tyr Thr Met Ile Tyr Arg Asn Leu Val Val Val Asn Gln
                100   105   110

Gln Glu Ser Ser Asp Ser Gly Thr Ser Val Ser Glu Asn Arg Cys His
            115   120   125

Leu Glu Gly Gly Ser Asp Gln Lys Asp Leu Val Gln Glu Leu Gln Glu
    130   135   140

Glu Lys Pro Ser Ser Ser His Leu Val Ser Arg Pro Ser Thr Ser Ser
145   150   155   160

Arg Arg Arg Ala Ile Ser Glu Thr Glu Glu Asn Ser Asp Glu Leu Ser
                165   170   175

Gly Glu Arg Gln Arg Lys Arg His Lys Ser Asp Ser Ile Ser Leu Ser
            180   185   190

Phe Asp Glu Ser Leu Ala Leu Cys Val Ile Arg Glu Ile Cys Cys Glu
            195   200   205

Arg Ser Ser Ser Ser Glu Ser Thr Gly Thr Pro Ser Asn Pro Asp Leu
    210   215   220

```
Asp Ala Gly Val Ser Glu His Ser Gly Asp Trp Leu Asp Gln Asp Ser
225             230             235             240

Val Ser Asp Gln Phe Ser Val Glu Phe Glu Val Glu Ser Leu Asp Ser
            245             250             255

Glu Asp Tyr Ser Leu Ser Glu Glu Gly Gln Glu Leu Ser Asp Glu Asp
            260             265             270

Asp Glu Val Tyr Gln Val Thr Val Tyr Gln Ala Gly Glu Ser Asp Thr
            275             280             285

Asp Ser Phe Glu Glu Asp Pro Glu Ile Ser Leu Ala Asp Tyr Trp Lys
    290             295             300

Cys Thr Ser Cys Asn Glu Met Asn Pro Pro Leu Pro Ser His Cys Asn
305             310             315             320

Arg Cys Trp Ala Leu Arg Glu Asn Trp Leu Pro Glu Asp Lys Gly Lys
            325             330             335

Asp Lys Gly Glu Ile Ser Glu Lys Ala Lys Leu Glu Asn Ser Thr Gln
            340             345             350

Ala Glu Glu Gly Phe Asp Val Pro Asp Cys Lys Lys Thr Ile Val Asn
            355             360             365

Asp Ser Arg Glu Ser Cys Val Glu Glu Asn Asp Asp Lys Ile Thr Gln
    370             375             380

Ala Ser Gln Ser Gln Glu Ser Glu Asp Tyr Ser Gln Pro Ser Thr Ser
385             390             395             400

Ser Ser Ile Ile Tyr Ser Ser Gln Glu Asp Val Lys Glu Phe Glu Arg
            405             410             415

Glu Glu Thr Gln Asp Lys Glu Glu Ser Val Glu Ser Ser Leu Pro Leu
            420             425             430

Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly
            435             440             445

Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys
    450             455             460

Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln
```

1036

465   470   475   480

Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro
                485   490

<210> 2603
<211> 950
<212> PRT
<213> Homo sapiens

<400> 2603

Met Gly Val Pro Ala Phe Phe Arg Trp Leu Ser Arg Lys Tyr Pro Ser
1   5   10   15

Ile Ile Val Asn Cys Val Glu Glu Lys Pro Lys Glu Cys Asn Gly Val
              20   25   30

Lys Ile Pro Val Asp Ala Ser Lys Pro Asn Pro Asn Asp Val Glu Phe
          35   40   45

Asp Asn Leu Tyr Leu Asp Met Asn Gly Ile Ile His Pro Cys Thr His
      50   55   60

Pro Glu Asp Lys Pro Ala Pro Lys Asn Glu Asp Glu Met Met Val Ala
65   70   75   80

Ile Phe Glu Tyr Ile Asp Arg Leu Phe Ser Ile Val Arg Pro Arg Arg
                85   90   95

Leu Leu Tyr Met Ala Ile Asp Gly Val Ala Pro Arg Ala Lys Met Asn
              100   105   110

Gln Gln Arg Ser Arg Arg Phe Arg Ala Ser Lys Glu Gly Met Glu Ala
          115   120   125

Ala Val Glu Lys Gln Arg Val Arg Glu Glu Ile Leu Ala Lys Gly Gly
      130   135   140

Phe Leu Pro Pro Glu Glu Ile Lys Glu Arg Phe Asp Ser Asn Cys Ile
145   150   155   160

Thr Pro Gly Thr Glu Phe Met Asp Asn Leu Ala Lys Cys Leu Arg Tyr
              165   170   175

Tyr Ile Ala Asp Arg Leu Asn Asn Asp Pro Gly Trp Lys Asn Leu Thr
          180   185   190

```
Val Ile Leu Ser Asp Ala Ser Ala Pro Gly Glu Gly Glu His Lys Ile
        195                 200                 205

Met Asp Tyr Ile Arg Arg Gln Arg Ala Gln Pro Asn His Asp Pro Asn
    210                 215                 220

Thr His His Cys Leu Cys Gly Ala Asp Ala Asp Leu Ile Met Leu Gly
225                 230                 235                 240

Leu Ala Thr His Glu Pro Asn Phe Thr Ile Ile Arg Glu Glu Phe Lys
            245                 250                 255

Pro Asn Lys Pro Lys Pro Cys Gly Leu Cys Asn Gln Phe Gly His Glu
            260                 265                 270

Val Lys Asp Cys Glu Gly Leu Pro Arg Glu Lys Lys Gly Lys His Asp
        275                 280                 285

Glu Leu Ala Asp Ser Leu Pro Cys Ala Glu Gly Glu Phe Ile Phe Leu
    290                 295                 300

Arg Leu Asn Val Leu Arg Glu Tyr Leu Glu Arg Glu Leu Thr Met Ala
305                 310                 315                 320

Ser Leu Pro Phe Thr Phe Asp Val Glu Arg Ser Ile Asp Asp Trp Val
            325                 330                 335

Phe Met Cys Phe Phe Val Gly Asn Asp Phe Leu Pro His Leu Pro Ser
            340                 345                 350

Leu Glu Ile Arg Glu Asn Ala Ile Asp Arg Leu Val Asn Ile Tyr Lys
        355                 360                 365

Asn Val Val His Lys Thr Gly Gly Tyr Leu Thr Glu Ser Gly Tyr Val
370                 375                 380

Asn Leu Gln Arg Val Gln Met Ile Met Leu Ala Val Gly Glu Val Glu
385                 390                 395                 400

Asp Ser Ile Phe Lys Lys Arg Lys Asp Asp Glu Asp Ser Phe Arg Arg
            405                 410                 415

Arg Gln Lys Glu Lys Arg Lys Arg Met Lys Arg Asp Gln Pro Ala Phe
        420                 425                 430
```

```
Thr Pro Ser Gly Ile Leu Thr Pro His Ala Leu Gly Ser Arg Asn Ser
        435                 440                 445

Pro Gly Ser Gln Val Ala Ser Asn Pro Arg Gln Ala Ala Tyr Glu Met
        450                 455                 460

Arg Met Gln Asn Asn Ser Ser Pro Ser Ile Ser Pro Asn Thr Ser Phe
465                 470                 475                 480

Thr Ser Asp Gly Ser Pro Ser Pro Leu Gly Gly Ile Lys Arg Lys Ala
                485                 490                 495

Glu Asp Ser Asp Ser Glu Pro Glu Pro Glu Asp Asn Val Arg Leu Trp
            500                 505                 510

Glu Ala Gly Trp Lys Gln Arg Tyr Tyr Lys Asn Lys Phe Asp Val Asp
        515                 520                 525

Ala Ala Asp Glu Lys Phe Arg Arg Lys Val Val Gln Ser Tyr Val Glu
        530                 535                 540

Gly Leu Cys Trp Val Leu Arg Tyr Tyr Tyr Gln Gly Cys Ala Ser Trp
545                 550                 555                 560

Lys Trp Tyr Tyr Pro Phe His Tyr Ala Pro Phe Ala Ser Asp Phe Glu
                565                 570                 575

Gly Ile Ala Asp Met Pro Ser Asp Phe Glu Lys Gly Thr Lys Pro Phe
                580                 585                 590

Lys Pro Leu Glu Gln Leu Met Gly Val Phe Pro Ala Ala Ser Gly Asn
        595                 600                 605

Phe Leu Pro Pro Ser Trp Arg Lys Leu Met Ser Asp Pro Asp Ser Ser
        610                 615                 620

Ile Ile Asp Phe Tyr Pro Glu Asp Phe Ala Ile Asp Leu Asn Gly Lys
625                 630                 635                 640

Lys Tyr Ala Trp Gln Gly Val Ala Leu Leu Pro Phe Val Asp Glu Arg
                645                 650                 655

Arg Leu Arg Ala Ala Leu Glu Glu Val Tyr Pro Asp Leu Thr Pro Glu
            660                 665                 670

Glu Thr Arg Arg Asn Ser Leu Gly Gly Asp Val Leu Phe Val Gly Lys
```

```
        675                  680                  685

His His Pro Leu His Asp Phe Ile Leu Glu Leu Tyr Gln Thr Gly Ser
    690                  695                  700

Thr Glu Pro Val Glu Val Pro Pro Glu Leu Cys His Gly Ile Gln Gly
705                  710                  715                  720

Lys Phe Ser Leu Asp Glu Glu Ala Ile Leu Pro Asp Gln Ile Val Cys
                725                  730                  735

Ser Pro Val Pro Met Leu Arg Asp Leu Thr Gln Asn Thr Val Val Ser
            740                  745                  750

Ile Asn Phe Lys Asp Pro Gln Phe Ala Glu Asp Tyr Ile Phe Lys Ala
            755                  760                  765

Val Met Leu Pro Gly Ala Arg Lys Pro Ala Ala Val Leu Lys Pro Ser
    770                  775                  780

Asp Trp Glu Lys Ser Ser Asn Gly Arg Gln Trp Lys Pro Gln Leu Gly
785                  790                  795                  800

Phe Asn Arg Asp Arg Arg Pro Val His Leu Asp Gln Ala Ala Phe Arg
                805                  810                  815

Thr Leu Gly His Val Met Pro Arg Gly Ser Gly Thr Gly Ile Tyr Ser
            820                  825                  830

Asn Ala Ala Pro Pro Pro Val Thr Tyr Gln Gly Asn Leu Tyr Arg Pro
            835                  840                  845

Leu Leu Arg Gly Gln Ala Gln Ile Pro Lys Leu Met Ser Asn Met Arg
    850                  855                  860

Pro Gln Asp Ser Trp Arg Gly Pro Pro Pro Leu Phe Gln Gln Gln Arg
865                  870                  875                  880

Phe Asp Arg Gly Val Gly Ala Glu Pro Leu Leu Pro Trp Asn Arg Met
                885                  890                  895

Leu Gln Thr Gln Asn Ala Ala Phe Gln Pro Asn Gln Tyr Gln Met Leu
            900                  905                  910

Ala Gly Pro Gly Gly Tyr Pro Pro Arg Arg Asp Asp Arg Gly Gly Arg
            915                  920                  925
```

```
Gln Gly Tyr Pro Arg Glu Gly Arg Lys Tyr Pro Leu Pro Pro Pro Ser
        930             935             940

Gly Arg Tyr Asn Trp Asn
945             950
```

<210> 2604
<211> 313
<212> PRT
<213> Homo sapiens

<400> 2604

```
Met Ser Gln Ser Arg His Arg Ala Glu Ala Pro Pro Leu Glu Arg Glu
1               5               10              15

Asp Ser Gly Thr Phe Ser Leu Gly Lys Met Ile Thr Ala Lys Pro Gly
            20              25              30

Lys Thr Pro Ile Gln Val Leu His Glu Tyr Gly Met Lys Thr Lys Asn
        35              40              45

Ile Pro Val Tyr Glu Cys Glu Arg Ser Asp Val Gln Ile His Val Pro
    50              55              60

Thr Phe Thr Phe Arg Val Thr Val Gly Asp Ile Thr Cys Thr Gly Glu
65              70              75              80

Gly Thr Ser Lys Lys Leu Ala Lys His Arg Ala Ala Glu Ala Ala Ile
            85              90              95

Asn Ile Leu Lys Ala Asn Ala Ser Ile Cys Phe Ala Val Pro Asp Pro
            100             105             110

Leu Met Pro Asp Pro Ser Lys Gln Pro Lys Asn Gln Leu Asn Pro Ile
        115             120             125

Gly Ser Leu Gln Glu Leu Ala Ile His His Gly Trp Arg Leu Pro Glu
    130             135             140

Tyr Thr Leu Ser Gln Glu Gly Gly Pro Ala His Lys Arg Glu Tyr Thr
145             150             155             160

Thr Ile Cys Arg Leu Glu Ser Phe Met Glu Thr Gly Lys Gly Ala Ser
                165             170             175
```

```
Lys Lys Gln Ala Lys Arg Asn Ala Ala Glu Lys Phe Leu Ala Lys Phe
            180                 185                 190

Ser Asn Ile Ser Pro Glu Asn His Ile Ser Leu Thr Asn Val Val Gly
            195                 200                 205

His Ser Leu Gly Cys Thr Trp His Ser Leu Arg Asn Ser Pro Gly Glu
    210                 215                 220

Lys Ile Asn Leu Leu Lys Arg Ser Leu Leu Ser Ile Pro Asn Thr Asp
225                 230                 235                 240

Tyr Ile Gln Leu Leu Ser Glu Ile Ala Lys Glu Gln Gly Phe Asn Ile
            245                 250                 255

Thr Tyr Leu Asp Ile Asp Glu Leu Ser Ala Asn Gly Gln Tyr Gln Cys
            260                 265                 270

Leu Ala Glu Leu Ser Thr Ser Pro Ile Thr Val Cys His Gly Ser Gly
            275                 280                 285

Ile Ser Cys Gly Asn Ala Gln Ser Asp Ala Ala His Asn Ala Leu Gln
    290                 295                 300

Tyr Leu Lys Ile Ile Ala Glu Arg Lys
305                 310
```

```
<210>  2605
<211>  198
<212>  PRT
<213>  Homo sapiens

<400>  2605
```

```
Met Ser Asn Val Arg Val Ser Asn Gly Ser Pro Ser Leu Glu Arg Met
1               5                   10                  15

Asp Ala Arg Gln Ala Glu His Pro Lys Pro Ser Ala Cys Arg Asn Leu
            20                  25                  30

Phe Gly Pro Val Asp His Glu Glu Leu Thr Arg Asp Leu Glu Lys His
            35                  40                  45

Cys Arg Asp Met Glu Glu Ala Ser Gln Arg Lys Trp Asn Phe Asp Phe
    50                  55                  60

Gln Asn His Lys Pro Leu Glu Gly Lys Tyr Glu Trp Gln Glu Val Glu
65                  70                  75                  80
```

Lys Gly Ser Leu Pro Glu Phe Tyr Tyr Arg Pro Pro Arg Pro Pro Lys
                 85   90   95

Gly Ala Cys Lys Val Pro Ala Gln Glu Ser Gln Asp Val Ser Gly Ser
             100   105   110

Arg Pro Ala Ala Pro Leu Ile Gly Ala Pro Ala Asn Ser Glu Asp Thr
         115   120   125

His Leu Val Asp Pro Lys Thr Asp Pro Ser Asp Ser Gln Thr Gly Leu
     130   135   140

Ala Glu Gln Cys Ala Gly Ile Arg Lys Arg Pro Ala Thr Asp Asp Ser
145   150   155   160

Ser Thr Gln Asn Lys Arg Ala Asn Arg Thr Glu Glu Asn Val Ser Asp
                 165   170   175

Gly Ser Pro Asn Ala Gly Ser Val Glu Gln Thr Pro Lys Lys Pro Gly
             180   185   190

Leu Arg Arg Arg Gln Thr
         195

<210> 2606
<211> 727
<212> PRT
<213> Homo sapiens

<400> 2606

Met Arg Pro Leu Leu Leu Leu Ala Leu Leu Gly Trp Leu Leu Leu Ala
1   5   10   15

Glu Ala Lys Gly Asp Ala Lys Pro Glu Asp Asn Leu Leu Val Leu Thr
             20   25   30

Val Ala Thr Lys Glu Thr Glu Gly Phe Arg Arg Phe Lys Arg Ser Ala
         35   40   45

Gln Phe Phe Asn Tyr Lys Ile Gln Ala Leu Gly Leu Gly Glu Asp Trp
     50   55   60

Asn Val Glu Lys Gly Thr Ser Ala Gly Gly Gly Gln Lys Val Arg Leu
65   70   75   80

Leu Lys Lys Ala Leu Glu Lys His Ala Asp Lys Glu Asp Leu Val Ile
                85   90   95

Leu Phe Thr Asp Ser Tyr Asp Val Leu Phe Ala Ser Gly Pro Arg Glu
                100   105   110

Leu Leu Lys Lys Phe Arg Gln Ala Arg Ser Gln Val Val Phe Ser Ala
            115   120   125

Glu Glu Leu Ile Tyr Pro Asp Arg Arg Leu Glu Thr Lys Tyr Pro Val
    130   135   140

Val Ser Asp Gly Lys Arg Phe Leu Gly Ser Gly Gly Phe Ile Gly Tyr
145   150   155   160

Ala Pro Asn Leu Ser Lys Leu Val Ala Glu Trp Glu Gly Gln Asp Ser
                165   170   175

Asp Ser Asp Gln Leu Phe Tyr Thr Lys Ile Phe Leu Asp Pro Glu Lys
                180   185   190

Arg Glu Gln Ile Asn Ile Thr Leu Asp His Arg Cys Arg Ile Phe Gln
        195   200   205

Asn Leu Asp Gly Ala Leu Asp Glu Val Val Leu Lys Phe Glu Met Gly
    210   215   220

His Val Arg Ala Arg Asn Leu Ala Tyr Asp Thr Leu Pro Val Leu Ile
225   230   235   240

His Gly Asn Gly Pro Thr Lys Leu Gln Leu Asn Tyr Leu Gly Asn Tyr
                245   250   255

Ile Pro Arg Phe Trp Thr Phe Glu Thr Gly Cys Thr Val Cys Asp Glu
                260   265   270

Gly Leu Arg Ser Leu Lys Gly Ile Gly Asp Glu Ala Leu Pro Thr Val
        275   280   285

Leu Val Gly Val Phe Ile Glu Gln Pro Thr Pro Phe Val Ser Leu Phe
    290   295   300

Phe Gln Arg Leu Leu Arg Leu His Tyr Pro Gln Lys His Met Arg Leu
305   310   315   320

Phe Ile His Asn His Glu Gln His His Lys Ala Gln Val Glu Glu Phe

1044

<div style="text-align: center">325   330   335</div>

Leu Ala Gln His Gly Ser Glu Tyr Gln Ser Val Lys Leu Val Gly Pro
        340   345   350

Glu Val Arg Met Ala Asn Ala Asp Ala Arg Asn Met Gly Ala Asp Leu
    355   360   365

Cys Arg Gln Asp Arg Ser Cys Thr Tyr Tyr Phe Ser Val Asp Ala Asp
    370   375   380

Val Ala Leu Thr Glu Pro Asn Ser Leu Arg Leu Ile Gln Gln Asn
385   390   395   400

Lys Asn Val Ile Ala Pro Leu Met Thr Arg His Gly Arg Leu Trp Ser
            405   410   415

Asn Phe Trp Gly Ala Leu Ser Ala Asp Gly Tyr Tyr Ala Arg Ser Glu
            420   425   430

Asp Tyr Val Asp Ile Val Gln Gly Arg Arg Val Gly Val Trp Asn Val
        435   440   445

Pro Tyr Ile Ser Asn Ile Tyr Leu Ile Lys Gly Ser Ala Leu Arg Gly
    450   455   460

Glu Leu Gln Ser Ser Asp Leu Phe His His Ser Lys Leu Asp Pro Asp
465   470   475   480

Met Ala Phe Cys Ala Asn Ile Arg Gln Gln Asp Val Phe Met Phe Leu
            485   490   495

Thr Asn Arg His Thr Leu Gly His Leu Leu Ser Leu Asp Ser Tyr Arg
            500   505   510

Thr Thr His Leu His Asn Asp Leu Trp Glu Val Phe Ser Asn Pro Glu
    515   520   525

Asp Trp Lys Glu Lys Tyr Ile His Gln Asn Tyr Thr Lys Ala Leu Ala
    530   535   540

Gly Lys Leu Val Glu Thr Pro Cys Pro Asp Val Tyr Trp Phe Pro Ile
545   550   555   560

Phe Thr Glu Val Ala Cys Asp Glu Leu Val Glu Glu Met Glu His Phe
            565   570   575

<div style="text-align: center">1045</div>

Gly Gln Trp Ser Leu Gly Asn Asn Lys Asp Asn Arg Ile Gln Gly Gly
            580   585   590

Tyr Glu Asn Val Pro Thr Ile Asp Ile His Met Asn Gln Ile Gly Phe
        595   600   605

Glu Arg Glu Trp His Lys Phe Leu Leu Glu Tyr Ile Ala Pro Met Thr
    610   615   620

Glu Lys Leu Tyr Pro Gly Tyr Tyr Thr Arg Ala Gln Phe Asp Leu Ala
625   630   635   640

Phe Val Val Arg Tyr Lys Pro Asp Glu Gln Pro Ser Leu Met Pro His
            645   650   655

His Asp Ala Ser Thr Phe Thr Ile Asn Ile Ala Leu Asn Arg Val Gly
            660   665   670

Val Asp Tyr Glu Gly Gly Gly Cys Arg Phe Leu Arg Tyr Asn Cys Ser
        675   680   685

Ile Arg Ala Pro Arg Lys Gly Trp Thr Leu Met His Pro Gly Arg Leu
    690   695   700

Thr His Tyr His Glu Gly Leu Pro Thr Thr Arg Gly Thr Arg Tyr Ile
705   710   715   720

Ala Val Ser Phe Val Asp Pro
                725

<210>   2607
<211>   537
<212>   PRT
<213>   Homo sapiens

<400>   2607

Met Ala Trp Arg Gly Ala Gly Pro Ser Val Pro Gly Ala Pro Gly Gly
1   5   10   15

Val Gly Leu Ser Leu Gly Leu Leu Leu Gln Leu Leu Leu Leu Leu Gly
            20   25   30

Pro Ala Arg Gly Phe Gly Asp Glu Glu Glu Arg Arg Cys Asp Pro Ile
            35   40   45

```
Arg Ile Ser Met Cys Gln Asn Leu Gly Tyr Asn Val Thr Lys Met Pro
    50              55              60

Asn Leu Val Gly His Glu Leu Gln Thr Asp Ala Glu Leu Gln Leu Thr
65              70              75              80

Thr Phe Thr Pro Leu Ile Gln Tyr Gly Cys Ser Ser Gln Leu Gln Phe
            85              90              95

Phe Leu Cys Ser Val Tyr Val Pro Met Cys Thr Glu Lys Ile Asn Ile
        100             105             110

Pro Ile Gly Pro Cys Gly Gly Met Cys Leu Ser Val Lys Arg Arg Cys
        115             120             125

Glu Pro Val Leu Lys Glu Phe Gly Phe Ala Trp Pro Glu Ser Leu Asn
    130             135             140

Cys Ser Lys Phe Pro Pro Gln Asn Asp His Asn His Met Cys Met Glu
145             150             155             160

Gly Pro Gly Asp Glu Glu Val Pro Leu Pro His Lys Thr Pro Ile Gln
            165             170             175

Pro Gly Glu Glu Cys His Ser Val Gly Thr Asn Ser Asp Gln Tyr Ile
            180             185             190

Trp Val Lys Arg Ser Leu Asn Cys Val Leu Lys Cys Gly Tyr Asp Ala
        195             200             205

Gly Leu Tyr Ser Arg Ser Ala Lys Glu Phe Thr Asp Ile Trp Met Ala
    210             215             220

Val Trp Ala Ser Leu Cys Phe Ile Ser Thr Ala Phe Thr Val Leu Thr
225             230             235             240

Phe Leu Ile Asp Ser Ser Arg Phe Ser Tyr Pro Glu Arg Pro Ile Ile
            245             250             255

Phe Leu Ser Met Cys Tyr Asn Ile Tyr Ser Ile Ala Tyr Ile Val Arg
            260             265             270

Leu Thr Val Gly Arg Glu Arg Ile Ser Cys Asp Phe Glu Glu Ala Ala
        275             280             285

Glu Pro Val Leu Ile Gln Glu Gly Leu Lys Asn Thr Gly Cys Ala Ile
```

1047

             290   295   300

    Ile Phe Leu Leu Met Tyr Phe Phe Gly Met Ala Ser Ser Ile Trp Trp
    305   310   315   320

    Val Ile Leu Thr Leu Thr Trp Phe Leu Ala Ala Gly Leu Lys Trp Gly
                      325   330   335

    His Glu Ala Ile Glu Met His Ser Ser Tyr Phe His Ile Ala Ala Trp
                      340   345   350

    Ala Ile Pro Ala Val Lys Thr Ile Val Ile Leu Ile Met Arg Leu Val
                  355   360   365

    Asp Ala Asp Glu Leu Thr Gly Leu Cys Tyr Val Gly Asn Gln Asn Leu
        370   375   380

    Asp Ala Leu Thr Gly Phe Val Val Ala Pro Leu Phe Thr Tyr Leu Val
    385   390   395   400

    Ile Gly Thr Leu Phe Ile Ala Ala Gly Leu Val Ala Leu Phe Lys Ile
                  405   410   415

    Arg Ser Asn Leu Gln Lys Asp Gly Thr Lys Thr Asp Lys Leu Glu Arg
                  420   425   430

    Leu Met Val Lys Ile Gly Val Phe Ser Val Leu Tyr Thr Val Pro Ala
                  435   440   445

    Thr Cys Val Ile Ala Cys Tyr Phe Tyr Glu Ile Ser Asn Trp Ala Leu
        450   455   460

    Phe Arg Tyr Ser Ala Asp Asp Ser Asn Met Ala Val Glu Met Leu Lys
    465   470   475   480

    Ile Phe Met Ser Leu Leu Val Gly Ile Thr Ser Gly Met Trp Ile Trp
                  485   490   495

    Ser Ala Lys Thr Leu His Thr Trp Gln Lys Cys Ser Asn Arg Leu Val
                  500   505   510

    Asn Ser Gly Lys Val Lys Arg Glu Lys Arg Gly Asn Gly Trp Val Lys
            515   520   525

    Pro Gly Lys Gly Ser Glu Thr Val Val
        530   535

<210>   2608
<211>   362
<212>   PRT
<213>   Homo sapiens

<400>   2608

Met Leu Val Met Ala Pro Arg Thr Val Leu Leu Leu Ser Ala Ala
1   5   10   15

Leu Ala Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
              20   25   30

Tyr Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser
          35   40   45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
      50   55   60

Ala Ser Pro Arg Glu Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65   70   75   80

Pro Glu Tyr Trp Asp Arg Asn Thr Gln Ile Tyr Lys Ala Gln Ala Gln
              85   90   95

Thr Asp Arg Glu Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
          100   105   110

Glu Ala Gly Ser His Thr Leu Gln Ser Met Tyr Gly Cys Asp Val Gly
          115   120   125

Pro Asp Gly Arg Leu Leu Arg Gly His Asp Gln Tyr Ala Tyr Asp Gly
      130   135   140

Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
145   150   155   160

Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu
              165   170   175

Ala Glu Gln Arg Arg Ala Tyr Leu Glu Gly Glu Cys Val Glu Trp Leu
          180   185   190

Arg Arg Tyr Leu Glu Asn Gly Lys Asp Lys Leu Glu Arg Ala Asp Pro
          195   200   205

```
Pro Lys Thr His Val Thr His His Pro Ile Ser Asp His Glu Ala Thr
    210             215             220

Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
225             230             235             240

Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
            245             250             255

Thr Arg Pro Ala Gly Asp Arg Thr Phe Gln Lys Trp Ala Ala Val Val
            260             265             270

Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu
        275             280             285

Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Ser
    290             295             300

Thr Val Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val
305             310             315             320

Val Val Ile Gly Ala Val Val Ala Ala Val Met Cys Arg Arg Lys Ser
            325             330             335

Ser Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys Ser Asp Ser
            340             345             350

Ala Gln Gly Ser Asp Val Ser Leu Thr Ala
            355             360
```

<210> 2609
<211> 350
<212> PRT
<213> Homo sapiens

<400> 2609

```
Met Glu Thr Asn Ser Ser Leu Pro Thr Asn Ile Ser Gly Gly Thr Pro
1               5               10              15

Ala Val Ser Ala Gly Tyr Leu Phe Leu Asp Ile Ile Thr Tyr Leu Val
            20              25              30

Phe Ala Val Thr Phe Val Leu Gly Val Leu Gly Asn Gly Leu Val Ile
        35              40              45

Trp Val Ala Gly Phe Arg Met Thr His Val Thr Thr Ile Ser Tyr
    50              55              60
```

```
Leu Asn Leu Ala Val Ala Asp Phe Cys Phe Thr Ser Thr Leu Pro Phe
65                  70              75              80


Phe Met Val Arg Lys Ala Met Gly Gly His Trp Pro Phe Gly Trp Phe
            85              90              95


Leu Cys Lys Phe Val Phe Thr Ile Val Asp Ile Asn Leu Phe Gly Ser
            100             105             110


Val Phe Leu Ile Ala Leu Ile Ala Leu Asp Arg Cys Val Cys Val Leu
            115             120             125


His Pro Val Trp Thr Gln Asn His Arg Thr Val Ser Leu Ala Lys Lys
130             135             140


Val Ile Ile Gly Pro Trp Val Met Ala Leu Leu Leu Thr Leu Pro Val
145             150             155             160


Ile Ile Arg Val Thr Thr Val Pro Gly Lys Thr Gly Thr Val Ala Cys
                165             170             175


Thr Phe Asn Phe Ser Pro Trp Thr Asn Asp Pro Lys Glu Arg Ile Asn
            180             185             190


Val Ala Val Ala Met Leu Thr Val Arg Gly Ile Ile Arg Phe Ile Ile
            195             200             205             -


Gly Phe Ser Ala Pro Met Ser Ile Val Ala Val Ser Tyr Gly Leu Ile
    210             215             220


Ala Thr Lys Ile His Lys Gln Gly Leu Ile Lys Ser Ser Arg Pro Leu
225             230             235             240


Arg Val Leu Ser Phe Val Ala Ala Ala Phe Phe Leu Cys Trp Ser Pro
            245             250             255


Tyr Gln Val Val Ala Leu Ile Ala Thr Val Arg Ile Arg Glu Leu Leu
            260             265             270


Gln Gly Met Tyr Lys Glu Ile Gly Ile Ala Val Asp Val Thr Ser Ala
        275             280             285


Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Met Leu Tyr Val Phe Met
    290             295             300
```

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Gly Gln Asp Phe Arg Glu Arg Leu Ile His Ala Leu Pro Ala Ser Leu
305   310   315   320

Glu Arg Ala Leu Thr Glu Asp Ser Thr Gln Thr Ser Asp Thr Ala Thr
                325   330   335

Asn Ser Thr Leu Pro Ser Ala Glu Val Glu Leu Gln Ala Lys
                340   345 .   350

<210> 2610
<211> 638
<212> PRT
<213> Homo sapiens

<400> 2610

Met Ser Ala Ser Ser Ser Gly Gly Ser Pro Arg Phe Pro Ser Cys Gly
1   5   10   15

Lys Asn Gly Val Thr Ser Leu Thr Gln Lys Lys Val Leu Arg Ala Pro
            20   25   30

Cys Gly Ala Pro Ser Val Thr Val Thr Lys Ser His Lys Arg Gly Met
        35   40   45

Lys Gly Asp Thr Val Asn Val Arg Arg Ser Val Arg Val Lys Thr Lys
    50   55   60

Asn Pro Pro His Cys Leu Glu Ile Thr Pro Pro Ser Ser Glu Lys Leu
65   70   75   80

Val Ser Val Met Arg Leu Ser Asp Leu Ser Thr Glu Asp Asp Asp Ser
            85   90   95

Gly His Cys Lys Met Asn Arg Tyr Asp Lys Lys Ile Asp Ser Leu Met
        100   105   110

Asn Ala Val Gly Cys Leu Lys Ser Glu Val Lys Met Gln Lys Gly Glu
        115   120   125

Arg Gln Met Ala Lys Arg Phe Leu Glu Glu Arg Lys Glu Glu Leu Glu
    130   135   140

Glu Val Ala His Glu Leu Ala Glu Thr Glu His Glu Asn Thr Val Leu
145   150   155   160

Arg His Asn Ile Glu Arg Met Lys Glu Glu Lys Asp Phe Thr Ile Leu

```
                165                 170                 175
```

Gln Lys Lys His Leu Gln Gln Glu Lys Glu Cys Leu Met Ser Lys Leu
            180   185   190

Val Glu Ala Glu Met Asp Gly Ala Ala Ala Ala Lys Gln Val Met Ala
            195   200   205

Leu Lys Asp Thr Ile Gly Lys Leu Lys Thr Glu Lys Gln Met Thr Cys
    210   215   220

Thr Asp Ile Asn Thr Leu Thr Arg Gln Lys Glu Leu Leu Leu Gln Lys
225   230   235   240

Leu Ser Thr Phe Glu Glu Thr Asn Arg Thr Leu Arg Asp Leu Leu Arg
            245   250   255

Glu Gln His Cys Lys Glu Asp Ser Glu Arg Leu Met Glu Gln Gln Gly
            260   265   270

Ala Leu Leu Lys Arg Leu Ala Glu Ala Asp Ser Glu Lys Ala Arg Leu
            275   280   285

Leu Leu Leu Leu Gln Asp Lys Asp Lys Glu Val Glu Glu Leu Leu Gln
    290   295   300

Glu Ile Gln Cys Glu Lys Ala Gln Ala Lys Thr Ala Ser Glu Leu Ser
305   310   315   320

Lys Ser Met Glu Ser Met Arg Gly His Leu Gln Ala Gln Leu Arg Ser
            325   330   335

Lys Glu Ala Glu Asn Ser Arg Leu Cys Met Gln Ile Lys Asn Leu Glu
            340   345   350

Arg Ser Gly Asn Gln His Lys Ala Glu Val Glu Ala Ile Met Glu Gln
            355   360   365

Leu Lys Glu Leu Lys Gln Lys Gly Asp Arg Asp Lys Glu Ser Leu Lys
    370   375   380

Lys Ala Ile Arg Ala Gln Lys Glu Arg Ala Glu Lys Ser Glu Glu Tyr
385   390   395   400

Ala Glu Gln Leu His Val Gln Leu Ala Asp Lys Asp Leu Tyr Val Ala
            405   410   415

```
Glu Ala Leu Ser Thr Leu Glu Ser Trp Arg Ser Arg Tyr Asn Gln Val
            420             425             430

Val Lys Glu Lys Gly Asp Leu Glu Leu Glu Ile Ile Val Leu Asn Asp
            435             440             445

Arg Val Thr Asp Leu Val Asn Gln Gln Gln Thr Leu Glu Glu Lys Met
    450             455             460

Arg Glu Asp Arg Asp Ser Leu Val Glu Arg Leu His Arg Gln Thr Ala
465             470             475             480

Glu Tyr Ser Ala Phe Lys Leu Glu Asn Glu Arg Leu Lys Ala Ser Phe
            485             490             495

Ala Pro Met Glu Asp Lys Leu Asn Gln Ala His Leu Glu Val Gln Gln
            500             505             510

Leu Lys Ala Ser Val Lys Asn Tyr Glu Gly Met Ile Asp Asn Tyr Lys
            515             520             525

Ser Gln Val Met Lys Thr Arg Leu Glu Ala Asp Glu Val Ala Ala Gln
    530             535             540

Leu Glu Arg Cys Asp Lys Glu Asn Lys Ile Leu Lys Asp Glu Met Asn
545             550             555             560

Lys Glu Ile Glu Ala Ala Arg Arg Gln Phe Gln Ser Gln Leu Ala Asp
            565             570             575

Leu Gln Gln Leu Pro Asp Ile Leu Lys Ile Thr Glu Ala Lys Leu Ala
            580             585             590

Glu Cys Gln Asp Gln Leu Gln Gly Tyr Glu Arg Lys Asn Ile Asp Leu
            595             600             605

Thr Ala Ile Ile Ser Asp Leu Arg Ser Arg Val Arg Asp Trp Gln Lys
    610             615             620

Gly Ser His Glu Leu Thr Arg Ala Gly Ala Arg Ile Pro Arg
625             630             635
```

```
<210> 2611
<211> 197
<212> PRT
```

<210> Homo sapiens

<400> 2611

Met Thr Leu Leu Pro Gly Leu Leu Phe Leu Thr Trp Leu His Thr Cys
1   5   10   15

Leu Ala His His Asp Pro Ser Leu Arg Gly His Pro His Ser His Gly
                20   25   30

Thr Pro His Cys Tyr Ser Ala Glu Glu Leu Pro Leu Gly Gln Ala Pro
        35   40   45

Pro His Leu Leu Ala Arg Gly Ala Lys Trp Gly Gln Ala Leu Pro Val
    50   55   60

Ala Leu Val Ser Ser Leu Glu Ala Ala Ser His Arg Gly Arg His Glu
65   70   75   80

Arg Pro Ser Ala Thr Thr Gln Cys Pro Val Leu Arg Pro Glu Glu Val
                85   90   95

Leu Glu Ala Asp Thr His Gln Arg Ser Ile Ser Pro Trp Arg Tyr Arg
                100   105   110

Val Asp Thr Asp Glu Asp Arg Tyr Pro Gln Lys Leu Ala Phe Ala Glu
        115   120   125

Cys Leu Cys Arg Gly Cys Ile Asp Ala Arg Thr Gly Arg Glu Thr Ala
    130   135   140

Ala Leu Asn Ser Val Arg Leu Leu Gln Ser Leu Leu Val Leu Arg Arg
145   150   155   160

Arg Pro Cys Ser Arg Asp Gly Ser Gly Leu Pro Thr Pro Gly Ala Phe
                165   170   175

Ala Phe His Thr Glu Phe Ile His Val Pro Val Gly Cys Thr Cys Val
                180   185   190

Leu Pro Arg Ser Val
        195

<210> 2612
<211> 570
<212> PRT
<213> Homo sapiens

<400> 2612

```
Met Asn Val Val Phe Ala Val Lys Gln Tyr Ile Ser Lys Met Ile Glu
1               5                   10              15

Asp Ser Gly Pro Gly Met Lys Val Leu Leu Met Asp Lys Glu Thr Thr
            20                  25              30

Gly Ile Val Ser Met Val Tyr Thr Gln Ser Glu Ile Leu Gln Lys Glu
        35                  40              45

Val Tyr Leu Phe Glu Arg Ile Asp Ser Gln Asn Arg Glu Ile Met Lys
    50                  55                  60

His Leu Lys Ala Ile Cys Phe Leu Arg Pro Thr Lys Glu Asn Val Asp
65                  70                  75              80

Tyr Ile Ile Gln Glu Leu Arg Arg Pro Lys Tyr Thr Ile Tyr Phe Ile
                85                  90                  95

Tyr Phe Ser Asn Val Ile Ser Lys Ser Asp Val Lys Ser Leu Ala Glu
            100                 105                 110

Ala Asp Glu Gln Glu Val Val Ala Glu Val Gln Glu Phe Tyr Gly Asp
        115                 120                 125

Tyr Ile Ala Val Asn Pro His Leu Phe Ser Leu Asn Ile Leu Gly Cys
    130                 135                 140

Cys Gln Gly Arg Asn Trp Asp Pro Ala Gln Leu Ser Arg Thr Thr Gln
145                 150                 155                 160

Gly Leu Thr Ala Leu Leu Leu Ser Leu Lys Lys Cys Pro Met Ile Arg
                165                 170                 175

Tyr Gln Leu Ser Ser Glu Ala Ala Lys Arg Leu Ala Glu Cys Val Lys
            180                 185                 190

Gln Val Ile Thr Lys Glu Tyr Glu Leu Phe Glu Phe Arg Arg Thr Glu
        195                 200                 205

Val Pro Pro Leu Leu Leu Ile Leu Asp Arg Cys Asp Asp Ala Ile Thr
    210                 215                 220

Pro Leu Leu Asn Gln Trp Thr Tyr Gln Ala Met Val His Glu Leu Leu
225                 230                 235                 240
```

Gly Ile Asn Asn Asn Arg Ile Asp Leu Ser Arg Val Pro Gly Ile Ser
            245   250   255

Lys Asp Leu Arg Glu Val Val Leu Ser Ala Glu Asn Asp Glu Phe Tyr
            260   265   270

Ala Asn Asn Met Tyr Leu Asn Phe Ala Glu Ile Gly Ser Asn Ile Lys
            275   280   285

Asn Leu Met Glu Asp Phe Gln Lys Lys Lys Pro Lys Glu Gln Gln Lys
    290   295   300

Leu Glu Ser Ile Ala Asp Met Lys Ala Phe Val Glu Asn Tyr Pro Gln
305   310   315   320

Phe Lys Lys Met Ser Gly Thr Val Ser Lys His Val Thr Val Val Gly
            325   330   335

Glu Leu Ser Arg Leu Val Ser Glu Arg Asn Leu Leu Glu Val Ser Glu
            340   345   350

Val Glu Gln Glu Leu Ala Cys Gln Asn Asp His Ser Ser Ala Leu Gln
    355   360   365

Asn Ile Lys Arg Leu Leu Gln Asn Pro Lys Val Thr Glu Phe Asp Ala
    370   375   380

Ala Arg Leu Val Met Leu Tyr Ala Leu His Tyr Glu Arg His Ser Ser
385   390   395   400

Asn Ser Leu Pro Gly Leu Met Met Asp Leu Arg Asn Lys Gly Val Ser
            405   410   415

Glu Lys Tyr Arg Lys Leu Val Ser Ala Val Val Glu Tyr Gly Gly Lys
            420   425   430

Arg Val Arg Gly Ser Asp Leu Phe Ser Pro Lys Asp Ala Val Ala Ile
            435   440   445

Thr Lys Gln Phe Leu Lys Gly Leu Lys Gly Val Glu Asn Val Tyr Thr
    450   455   460

Gln His Gln Pro Phe Leu His Glu Thr Leu Asp His Leu Ile Lys Gly
465   470   475   480

Arg Leu Lys Glu Asn Leu Tyr Pro Tyr Leu Gly Pro Ser Thr Leu Arg
            485   490   495

Asp Arg Pro Gln Asp Ile Ile Val Phe Val Ile Gly Gly Ala Thr Tyr
            500   505   510

Glu Glu Ala Leu Thr Val Tyr Asn Leu Asn Arg Thr Thr Pro Gly Val
            515   520   525

Arg Ile Val Leu Gly Gly Thr Thr Val His Asn Thr Lys Ser Phe Leu
        530   535   540

Glu Glu Val Leu Ala Ser Gly Leu His Ser Arg Ser Lys Glu Ser Ser
545   550   555   560

Gln Val Thr Ser Arg Ser Ala Ser Arg Arg
            565   570

<210> 2613
<211> 474
<212> PRT
<213> Homo sapiens

<400> 2613

Met Thr Ile Leu Thr Tyr Pro Phe Lys Asn Leu Pro Thr Ala Ser Lys
1   5   10   15

Trp Ala Leu Arg Phe Ser Ile Arg Pro Leu Ser Cys Ser Ser Gln Leu
            20   25   30

Arg Ala Ala Pro Ala Val Gln Thr Lys Thr Lys Lys Thr Leu Ala Lys
        35   40   45

Pro Asn Ile Arg Asn Val Val Val Asp Gly Val Arg Thr Pro Phe
        50   55   60

Leu Leu Ser Gly Thr Ser Tyr Lys Asp Leu Met Pro His Asp Leu Ala
65   70   75   80

Arg Ala Ala Leu Thr Gly Leu Leu His Arg Thr Ser Val Pro Lys Glu
            85   90   95

Val Val Asp Tyr Ile Ile Phe Gly Thr Val Ile Gln Glu Val Lys Thr
            100   105   110

Ser Asn Val Ala Arg Glu Ala Ala Leu Gly Ala Gly Phe Ser Asp Lys
            115   120   125

1058

Thr Pro Ala His Thr Val Thr Met Ala Cys Ile Ser Ala Asn Gln Ala
    130   135   140

Met Thr Thr Gly Val Gly Leu Ile Ala Ser Gly Gln Cys Asp Val Ile
145   150   155   160

Val Ala Gly Gly Val Glu Leu Met Ser Asp Val Pro Ile Arg His Ser
            165   170   175

Arg Lys Met Arg Lys Leu Met Leu Asp Leu Asn Lys Ala Lys Ser Met
        180   185   190

Gly Gln Arg Leu Ser Leu Ile Ser Lys Phe Arg Phe Asn Phe Leu Ala
        195   200   205

Pro Glu Leu Pro Ala Val Ser Glu Phe Ser Thr Ser Glu Thr Met Gly
    210   215   220

His Ser Ala Asp Arg Leu Ala Ala Ala Phe Ala Val Ser Arg Leu Glu
225   230   235   240

Gln Asp Glu Tyr Ala Leu Arg Ser His Ser Leu Ala Lys Lys Ala Gln
            245   250   255

Asp Glu Gly Leu Leu Ser Asp Val Val Pro Phe Lys Val Pro Gly Lys
            260   265   270

Asp Thr Val Thr Lys Asp Asn Gly Ile Arg Pro Ser Ser Leu Glu Gln
        275   280   285

Met Ala Lys Leu Lys Pro Ala Phe Ile Lys Pro Tyr Gly Thr Val Thr
    290   295   300

Ala Ala Asn Ser Ser Phe Leu Thr Asp Gly Ala Ser Ala Met Leu Ile
305   310   315   320

Met Ala Glu Glu Lys Ala Leu Ala Met Gly Tyr Lys Pro Lys Ala Tyr
            325   330   335

Leu Arg Asp Phe Met Tyr Val Ser Gln Asp Pro Lys Asp Gln Leu Leu
            340   345   350

Leu Gly Pro Thr Tyr Ala Thr Pro Lys Val Leu Glu Lys Ala Gly Leu
            355   360   365

```
Thr Met Asn Asp Ile Asp Ala Phe Glu Phe His Glu Ala Phe Ser Gly
    370             375             380

Gln Ile Leu Ala Asn Phe Lys Ala Met Asp Ser Asp Trp Phe Ala Glu
385             390             395             400

Asn Tyr Met Gly Arg Lys Thr Lys Val Gly Leu Pro Pro Leu Glu Lys
            405             410             415

Phe Asn Asn Trp Gly Gly Ser Leu Ser Leu Gly His Pro Phe Gly Ala
            420             425             430

Thr Gly Cys Arg Leu Val Met Ala Ala Ala Asn Arg Leu Arg Lys Glu
        435             440             445

Gly Gly Gln Tyr Gly Leu Val Ala Ala Cys Ala Ala Gly Gly Gln Gly
    450             455             460

His Ala Met Ile Val Glu Ala Tyr Pro Lys
465             470
```

```
<210>  2614
<211>  793
<212>  PRT
<213>  Homo sapiens

<400>  2614
```

```
Met Glu Ser Arg Ala Glu Gly Gly Ser Pro Ala Val Phe Asp Trp Phe
1               5               10              15

Phe Glu Ala Ala Cys Pro Ala Ser Leu Gln Glu Asp Pro Pro Ile Leu
            20              25              30

Arg Gln Phe Pro Pro Asp Phe Arg Asp Gln Glu Ala Met Gln Met Val
        35              40              45

Pro Lys Phe Cys Phe Pro Phe Asp Val Glu Arg Glu Pro Pro Ser Pro
    50              55              60

Ala Val Gln His Phe Thr Phe Ala Leu Thr Asp Leu Ala Gly Asn Arg
65              70              75              80

Arg Phe Gly Phe Cys Arg Leu Arg Ala Gly Thr Gln Ser Cys Leu Cys
            85              90              95

Ile Leu Ser His Leu Pro Trp Phe Glu Val Phe Tyr Lys Leu Leu Asn
```

```
                    100                    105                    110


      Thr Val Gly Asp Leu Leu Ala Gln Asp Gln Val Thr Glu Ala Glu Glu
              115                 120                 125


      Leu Leu Gln Asn Leu Phe Gln Gln Ser Leu Ser Gly Pro Gln Ala Ser
              130                 135                 140


      Val Gly Leu Glu Leu Gly Ser Gly Val Thr Val Ser Ser Gly Gln Gly
      145                 150                 155                 160


      Ile Pro Pro Pro Thr Arg Gly Asn Ser Lys Pro Leu Ser Cys Phe Val
                      165                 170                 175


      Ala Pro Asp Ser Gly Arg Leu Pro Ser Ile Pro Glu Asn Arg Asn Leu
                  180                 185                 190


      Thr Glu Leu Val Val Ala Val Thr Asp Glu Asn Ile Val Gly Leu Phe
              195                 200                 205


      Ala Ala Leu Leu Ala Glu Arg Arg Val Leu Leu Thr Ala Ser Lys Leu
      210                 215                 220


      Ser Thr Leu Thr Ser Cys Val His Ala Ser Cys Ala Leu Leu Tyr Pro
      225                 230                 235                 240


      Met Arg Trp Glu His Val Leu Ile Pro Thr Leu Pro Pro His Leu Leu
                      245                 250                 255


      Asp Tyr Cys Cys Ala Pro Met Pro Tyr Leu Ile Gly Val His Ala Ser
                  260                 265                 270


      Leu Ala Glu Arg Val Arg Glu Lys Ala Leu Glu Asp Val Val Val Leu
              275                 280                 285


      Asn Val Asp Ala Asn Thr Leu Glu Thr Thr Phe Asn Asp Val Gln Ala
          290                 295                 300


      Leu Pro Pro Asp Val Val Ser Leu Leu Arg Leu Arg Leu Arg Lys Val
      305                 310                 315                 320


      Ala Leu Ala Pro Gly Glu Gly Val Ser Arg Leu Phe Leu Lys Ala Gln
                  325                 330                 335


      Ala Leu Leu Phe Gly Gly Tyr Arg Asp Ala Leu Val Cys Ser Pro Gly
                  340                 345                 350
```

```
Gln Pro Val Thr Phe Ser Glu Glu Val Phe Leu Ala Gln Lys Pro Gly
        355                 360                 365

Ala Pro Leu Gln Ala Phe His Arg Arg Ala Val His Leu Gln Leu Phe
    370                 375                 380

Lys Gln Phe Ile Glu Ala Arg Leu Glu Lys Leu Asn Lys Gly Glu Gly
385                 390                 395                 400

Phe Ser Asp Gln Phe Glu Gln Glu Ile Thr Gly Cys Gly Ala Ser Pro
            405                 410                 415

Gly Ala Leu Arg Ser Tyr Gln Leu Trp Ala Asp Asn Leu Lys Lys Gly
            420                 425                 430

Gly Gly Ala Leu Leu His Ser Val Lys Ala Lys Thr Gln Pro Ala Val
        435                 440                 445

Lys Asn Met Tyr Arg Ser Ala Lys Ser Gly Leu Lys Gly Val Gln Ser
    450                 455                 460

Leu Leu Met Tyr Lys Asp Gly Asp Ser Val Leu Gln Arg Gly Gly Ser
465                 470                 475                 480

Leu Arg Ala Pro Ala Leu Pro Ser Arg Ser Asp Arg Leu Gln Gln Arg
            485                 490                 495

Leu Pro Ile Thr Gln His Phe Gly Lys Asn Arg Pro Leu Arg Pro Ser
            500                 505                 510

Arg Arg Arg Gln Leu Glu Glu Gly Thr Ser Glu Pro Pro Gly Ala Gly
        515                 520                 525

Thr Pro Pro Leu Ser Pro Glu Asp Glu Gly Cys Pro Trp Ala Glu Glu
    530                 535                 540

Ala Leu Asp Ser Ser Phe Leu Gly Ser Gly Glu Glu Leu Asp Leu Leu
545                 550                 555                 560

Ser Glu Ile Leu Asp Ser Leu Ser Met Gly Ala Lys Ser Ala Gly Ser
            565                 570                 575

Leu Arg Pro Ser Gln Ser Leu Asp Cys Cys His Arg Gly Asp Leu Asp
        580                 585                 590
```

```
Ser Cys Phe Ser Leu Pro Asn Ile Leu Arg Trp Gln Pro Asp Asp Lys
        595                 600                 605


Lys Leu Pro Glu Pro Glu Pro Gln Pro Leu Ser Leu Pro Ser Leu Gln
    610                 615                 620


Asn Ala Ser Ser Leu Asp Ala Thr Ser Ser Ser Lys Asp Ser Arg Ser
625                 630                 635                 640


Gln Leu Ile Pro Ser Glu Ser Asp Gln Glu Val Thr Ser Pro Ser Gln
                645                 650                 655


Ser Ser Thr Ala Ser Ala Asp Pro Ser Ile Trp Gly Asp Pro Lys Pro
            660                 665                 670


Ser Pro Leu Thr Glu Pro Leu Ile Leu His Leu Thr Pro Ser His Lys
        675                 680                 685


Ala Ala Glu Asp Phe Thr Ala Gln Glu Asn Pro Thr Pro Trp Leu Ser
    690                 695                 700


Thr Ala Pro Thr Glu Pro Ser Pro Pro Glu Ser Pro Gln Ile Leu Ala
705                 710                 715                 720


Pro Thr Lys Pro Asn Phe Asp Ile Ala Trp Thr Ser Gln Pro Leu Asp
            725                 730                 735


Pro Ser Ser Asp Pro Ser Ser Leu Glu Asp Pro Arg Ala Arg Pro Pro
            740                 745                 750


Lys Ala Leu Leu Ala Glu Arg Ala His Leu Gln Pro Arg Glu Glu Pro
        755                 760                 765


Gly Ala Leu Asn Ser Pro Ala Thr Pro Thr Ser Asn Cys Gln Lys Ser
    770                 775                 780


Gln Pro Ser Lys Pro Ala Gln Ser Arg
785                 790


<210>  2615
<211>  83
<212>  PRT
<213>  Homo sapiens

<400>  2615

Met Ser Phe Phe Gln Leu Leu Met Lys Arg Lys Glu Leu Ile Pro Leu
```

```
 1                 5                    10                      15

   Val Val Phe Met Thr Val Ala Ala Gly Gly Ala Ser Ser Phe Ala Val
               20              25              30

   Tyr Ser Leu Trp Lys Thr Asp Val Ile Leu Asp Arg Lys Lys Asn Pro
           35              40              45

   Glu Pro Trp Glu Thr Val Asp Pro Thr Val Pro Gln Lys Leu Ile Thr
       50              55              60

   Ile Asn Gln Gln Trp Lys Pro Ile Glu Glu Leu Gln Asn Val Gln Arg
   65              70              75              80

   Val Thr Lys
```

```
   Met Gly Ile Ser Thr Val Ile Leu Glu Met Cys Leu Leu Trp Gly Gln
   1               5                   10                  15

   Val Leu Ser Thr Gly Gly Trp Ile Pro Arg Thr Thr Asp Tyr Ala Ser
               20              25              30

   Leu Ile Pro Ser Glu Val Pro Leu Asp Gln Thr Val Ala Glu Gly Ser
           35              40              45

   Pro Phe Pro Ser Glu Ser Thr Leu Glu Ser Thr Ala Ala Glu Gly Ser
       50              55              60

   Pro Ile Ser Leu Glu Ser Thr Leu Glu Ser Thr Val Ala Glu Gly Ser
   65              70              75              80

   Leu Ile Pro Ser Glu Ser Thr Leu Glu Ser Thr Val Ala Glu Gly Ser
               85              90              95

   Asp Ser Gly Leu Ala Leu Arg Leu Val Asn Gly Asp Gly Arg Cys Gln
               100             105             110

   Gly Arg Val Glu Ile Leu Tyr Arg Gly Ser Trp Gly Thr Val Cys Asp
               115             120             125
```

```
Asp Ser Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg Gln Leu Gly
    130             135             140

Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Trp Phe Gly Gln Gly
145             150             155             160

Ser Gly Pro Ile Ala Leu Asp Asp Val Arg Cys Ser Gly His Glu Ser
            165             170             175

Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly
            180             185             190

His Gly Glu Asp Ala Gly Val Ile Cys Ser Ala Ala Gln Pro Gln Ser
        195             200             205

Thr Leu Arg Pro Glu Ser Trp Pro Val Arg Ile Ser Pro Pro Val Pro
    210             215             220

Thr Glu Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly Gly
225             230             235             240

Asp Arg Cys Arg Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp Gly
            245             250             255

Thr Val Cys Asp Asp Tyr Trp Asp Thr Asn Asp Ala Asn Val Val Cys
        260             265             270

Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Gln
        275             280             285

Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser
    290             295             300

Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Thr
305             310             315             320

His Asn Cys Gly His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala Pro
            325             330             335

Gln Ser Arg Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr Ser His Ala
        340             345             350

Ser Thr Ala Gly Pro Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly
    355             360             365
```

```
Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp
    370             375             380

Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Ser Asp Ala Asn Val Val
385             390             395             400

Cys Arg Gln Leu Gly Cys Gly Trp Ala Thr Ser Ala Pro Gly Asn Ala
            405             410             415

Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys
            420             425             430

Ser Gly Tyr Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu
        435             440             445

Ser His Asn Cys Gln His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala
    450             455             460

Ala His Ser Trp Ser Thr Pro Ser Pro Asp Thr Leu Pro Thr Ile Thr
465             470             475             480

Leu Pro Ala Ser Thr Val Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu
            485             490             495

Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg
            500             505             510

Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala
        515             520             525

Asn Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Met Leu Ala Pro
    530             535             540

Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp
545             550             555             560

Val Arg Cys Ser Gly Asn Glu Ser Tyr Leu Trp Ser Cys Pro His Asn
            565             570             575

Gly Trp Leu Ser His Asn Cys Gly His Ser Glu Asp Ala Gly Val Ile
        580             585             590

Cys Ser Gly Pro Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly Gly
        595             600             605

Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp Gly
```

```
        610                      615                      620
```

Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala Asn Val Val Cys
625   630   635   640

Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Arg
                645   650   655

Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser
                660   665   670

Gly His Glu Ser Tyr Leu Trp Ser Cys Pro Asn Asn Gly Trp Leu Ser
            675   680   685

His Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys Ser Ala Ala
        690   695   700

Gln Ser Arg Ser Thr Pro Arg Pro Asp Thr Leu Ser Thr Ile Thr Leu
705   710   715   720

Pro Pro Ser Thr Val Gly Ser Glu Ser Ser Leu Thr Leu Arg Leu Val
                725   730   735

Asn Gly Ser Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly
                740   745   750

Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Asn Asp Ala Asn
            755   760   765

Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly
    770   775   780

Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp Val
785   790   795   800

Arg Cys Ser Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly
                805   810   815

Trp Leu Ser His Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys
            820   825   830

Ser Val Ser Gln Ser Arg Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr
    835   840   845

Ser His Ala Ser Thr Ala Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu
850   855   860

```
Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg
865             870         875                 880

Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp Thr Ser Asp Ala
            885         890             895

Asn Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Thr Ser Ala Pro
        900             905             910

Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp
        915             920         925

Val Arg Cys Ser Gly Tyr Glu Ser Tyr Leu Trp Ser Cys Pro His Asn
930             935             940

Gly Trp Leu Ser His Asn Cys Gln His Ser Glu Asp Ala Gly Val Ile
945             950             955             960

Cys Ser Ala Ala His Ser Trp Ser Thr Pro Ser Pro Asp Thr Leu Pro
            965             970             975

Thr Ile Thr Leu Pro Ala Ser Thr Val Gly Ser Glu Ser Ser Leu Ala
        980             985             990

Leu Arg Leu Val Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val
        995             1000            1005

Leu Tyr Gln Gly Ser Trp Gly Thr Val Cys Asp Asp Ser Trp Asp
    1010            1015            1020

Thr Asn Asp Ala Asn Val Val Cys Arg Gln Pro Gly Cys Gly Trp
    1025            1030            1035

Ala Met Ser Ala Pro Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly
    1040            1045            1050

Pro Ile Val Leu Asp Asp Val Arg Cys Ser Gly His Glu Ser Tyr
    1055            1060            1065

Pro Trp Ser Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly
    1070            1075            1080

His Ser Glu Asp Ala Gly Val Ile Cys Ser Ala Ser Gln Ser Arg
    1085            1090            1095
```

Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr Ser His Ala Ser Thr
    1100   1105   1110

Ala Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu Val Asn Gly Gly
    1115   1120   1125

Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg Gly Ser Trp
    1130   1135   1140

Gly Thr Val Cys Asp Asp Tyr Trp Asp Thr Asn Asp Ala Asn Val
    1145   1150   1155

Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly
    1160   1165   1170

Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val Leu Asp Asp
    1175   1180   1185

Val Arg Cys Ser Gly His Glu Ser Tyr Leu Trp Ser Cys Pro His
    1190   1195   1200

Asn Gly Trp Leu Ser His Asn Cys Gly His His Glu Asp Ala Gly
    1205   1210   1215

Val Ile Cys Ser Ala Ser Gln Ser Gln Pro Thr Pro Ser Pro Asp
    1220   1225   1230

Thr Trp Pro Thr Ser His Ala Ser Thr Ala Gly Ser Glu Ser Ser
    1235   1240   1245

Leu Ala Leu Arg Leu Val Asn Gly Gly Asp Arg Cys Gln Gly Arg
    1250   1255   1260

Val Glu Val Leu Tyr Arg Gly Ser Trp Gly Thr Val Cys Asp Asp
    1265   1270   1275

Tyr Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg Gln Leu Gly
    1280   1285   1290

Cys Gly Trp Ala Thr Ser Ala Pro Gly Asn Ala Arg Phe Gly Gln
    1295   1300   1305

Gly Ser Gly Pro Ile Val Leu Asp Asp Val Arg Cys Ser Gly His
    1310   1315   1320

1069

Glu Ser Tyr Leu Trp Ser Cys Pro His Asn Gly Trp Leu Ser His
    1325   1330   1335

Asn Cys Gly His His Glu Asp Ala Gly Val Ile Cys Ser Ala Ser
    1340   1345   1350

Gln Ser Gln Pro Thr Pro Ser Pro Asp Thr Trp Pro Thr Ser His
    1355   1360   1365

Ala Ser Thr Ala Gly Ser Glu Ser Ser Leu Ala Leu Arg Leu Val
    1370   1375   1380

Asn Gly Gly Asp Arg Cys Gln Gly Arg Val Glu Val Leu Tyr Arg
    1385   1390   1395

Gly Ser Trp Gly Thr Val Cys Asp Asp Tyr Trp Asp Thr Asn Asp
    1400   1405   1410

Ala Asn Val Val Cys Arg Gln Leu Gly Cys Gly Trp Ala Thr Ser
    1415   1420   1425

Ala Pro Gly Asn Ala Arg Phe Gly Gln Gly Ser Gly Pro Ile Val
    1430   1435   1440

Leu Asp Asp Val Arg Cys Ser Gly His Glu Ser Tyr Leu Trp Ser
    1445   1450   1455

Cys Pro His Asn Gly Trp Leu Ser His Asn Cys Gly His His Glu
    1460   1465   1470

Asp Ala Gly Val Ile Cys Ser Ala Ser Gln Ser Gln Pro Thr Pro
    1475   1480   1485

Ser Pro Asp Thr Trp Pro Thr Ser Arg Ala Ser Thr Ala Gly Ser
    1490   1495   1500

Glu Ser Thr Leu Ala Leu Arg Leu Val Asn Gly Gly Asp Arg Cys
    1505   1510   1515

Arg Gly Arg Val Glu Val Leu Tyr Gln Gly Ser Trp Gly Thr Val
    1520   1525   1530

Cys Asp Asp Tyr Trp Asp Thr Asn Asp Ala Asn Val Val Cys Arg
    1535   1540   1545

Gln Leu Gly Cys Gly Trp Ala Met Ser Ala Pro Gly Asn Ala Gln

```
        1550                    1555                    1560


Phe Gly  Gln Gly Ser Gly Pro  Ile Val Leu Asp Asp  Val Arg Cys
        1565                    1570                    1575


Ser Gly  His Glu Ser Tyr Leu  Trp Ser Cys Pro His  Asn Gly Trp
        1580                    1585                    1590


Leu Ser  His Asn Cys Gly His  His Glu Asp Ala Gly  Val Ile Cys
        1595                    1600                    1605


Ser Ala  Ala Gln Ser Gln Ser  Thr Pro Arg Pro Asp  Thr Trp Leu
        1610                    1615                    1620


Thr Thr  Asn Leu Pro Ala Leu  Thr Val Gly Ser Glu  Ser Ser Leu
        1625                    1630                    1635


Ala Leu  Arg Leu Val Asn Gly  Gly Asp Arg Cys Arg  Gly Arg Val
        1640                    1645                    1650


Glu Val  Leu Tyr Arg Gly Ser  Trp Gly Thr Val Cys  Asp Asp Ser
        1655                    1660                    1665


Trp Asp  Thr Asn Asp Ala Asn  Val Val Cys Arg Gln  Leu Gly Cys
        1670                    1675                    1680


Gly Trp  Ala Met Ser Ala Pro  Gly Asn Ala Arg Phe  Gly Gln Gly
        1685                    1690                    1695


Ser Gly  Pro Ile Val Leu Asp  Asp Val Arg Cys Ser  Gly Asn Glu
        1700                    1705                    1710


Ser Tyr  Leu Trp Ser Cys Pro  His Lys Gly Trp Leu  Thr His Asn
        1715                    1720                    1725


Cys Gly  His His Glu Asp Ala  Gly Val Ile Cys Ser  Ala Thr Gln
        1730                    1735                    1740


Ile Asn  Ser Thr Thr Thr Asp  Trp Trp His Pro Thr  Thr Thr Thr
        1745                    1750                    1755


Thr Ala  Arg Pro Ser Ser Asn  Cys Gly Gly Phe Leu  Phe Tyr Ala
        1760                    1765                    1770


Ser Gly  Thr Phe Ser Ser Pro  Ser Tyr Pro Ala Tyr  Tyr Pro Asn
        1775                    1780                    1785
```

```
Asn Ala  Lys Cys Val Trp Glu  Ile Glu Val Asn Ser  Gly Tyr Arg
    1790                  1795             1800

Ile Asn  Leu Gly Phe Ser Asn  Leu Lys Leu Glu Ala  His His Asn
    1805                  1810             1815

Cys Ser  Phe Asp Tyr Val Glu  Ile Phe Asp Gly Ser  Leu Asn Ser
    1820                  1825             1830

Ser Leu  Leu Leu Gly Lys Ile  Cys Asn Asp Thr Arg  Gln Ile Phe
    1835                  1840             1845

Thr Ser  Ser Tyr Asn Arg Met  Thr Ile His Phe Arg  Ser Asp Ile
    1850                  1855             1860

Ser Phe  Gln Asn Thr Gly Phe  Leu Ala Trp Tyr Asn  Ser Phe Pro
    1865                  1870             1875

Ser Asp  Ala Thr Leu Arg Leu  Val Asn Leu Asn Ser  Ser Tyr Gly
    1880                  1885             1890

Leu Cys  Ala Gly Arg Val Glu  Ile Tyr His Gly Gly  Thr Trp Gly
    1895                  1900             1905

Thr Val  Cys Asp Asp Ser Trp  Thr Ile Gln Glu Ala  Glu Val Val
    1910                  1915             1920

Cys Arg  Gln Leu Gly Cys Gly  Arg Ala Val Ser Ala  Leu Gly Asn
    1925                  1930             1935

Ala Tyr  Phe Gly Ser Gly Ser  Gly Pro Ile Thr Leu  Asp Asp Val
    1940                  1945             1950

Glu Cys  Ser Gly Thr Glu Ser  Thr Leu Trp Gln Cys  Arg Asn Arg
    1955                  1960             1965

Gly Trp  Phe Ser His Asn Cys  Asn His Arg Glu Asp  Ala Gly Val
    1970                  1975             1980

Ile Cys  Ser Gly Asn His Leu  Ser Thr Pro Ala Pro  Phe Leu Asn
    1985                  1990             1995

Ile Thr  Arg Pro Asn Thr Asp  Tyr Ser Cys Gly Gly  Phe Leu Ser
    2000                  2005             2010
```

Gln Pro Ser Gly Asp Phe Ser Ser Pro Phe Tyr Pro Gly Asn Tyr
    2015   2020   2025

Pro Asn Asn Ala Lys Cys Val Trp Asp Ile Glu Val Gln Asn Asn
    2030   2035   2040

Tyr Arg Val Thr Val Ile Phe Arg Asp Val Gln Leu Glu Gly Gly
    2045   2050   2055

Cys Asn Tyr Asp Tyr Ile Glu Val Phe Asp Gly Pro Tyr Arg Ser
    2060   2065   2070

Ser Pro Leu Ile Ala Arg Val Cys Asp Gly Ala Arg Gly Ser Phe
    2075   2080   2085

Thr Ser Ser Ser Asn Phe Met Ser Ile Arg Phe Ile Ser Asp His
    2090   2095   2100

Ser Ile Thr Arg Arg Gly Phe Arg Ala Glu Tyr Tyr Ser Ser Pro
    2105   2110   2115

Ser Asn Asp Ser Thr Asn Leu Leu Cys Leu Pro Asn His Met Gln
    2120   2125   2130

Ala Ser Val Ser Arg Ser Tyr Leu Gln Ser Leu Gly Phe Ser Ala
    2135   2140   2145

                         ،

Ser Asp Leu Val Ile Ser Thr Trp Asn Gly Tyr Tyr Glu Cys Arg
    2150   2155   .   2160

Pro Gln Ile Thr Pro Asn Leu Val Ile Phe Thr Ile Pro Tyr Ser
    2165   2170   2175

Gly Cys Gly Thr Phe Lys Gln Ala Asp Asn Asp Thr Ile Asp Tyr
    2180   2185   2190

Ser Asn Phe Leu Thr Ala Ala Val Ser Gly Gly Ile Ile Lys Arg
    2195   2200   2205

Arg Thr Asp Leu Arg Ile His Val Ser Cys Arg Met Leu Gln Asn
    2210   2215   2220

Thr Trp Val Asp Thr Met Tyr Ile Ala Asn Asp Thr Ile His Val
    2225   2230   2235

```
Ala Asn   Asn Thr Ile Gln Val   Glu Glu Val Gln Tyr   Gly Asn Phe
    2240                  2245                  2250


Asp Val   Asn Ile Ser Phe Tyr   Thr Ser Ser Ser Phe   Leu Tyr Pro
    2255                  2260                  2265


Val Thr   Ser Arg Pro Tyr Tyr   Val Asp Leu Asn Gln   Asp Leu Tyr
    2270                  2275                  2280


Val Gln   Ala Glu Ile Leu His   Ser Asp Ala Val Leu   Thr Leu Phe
    2285                  2290                  2295


Val Asp   Thr Cys Val Ala Ser   Pro Tyr Ser Asn Asp   Phe Thr Ser
    2300                  2305                  2310


Leu Thr   Tyr Asp Leu Ile Arg   Ser Gly Cys Val Arg   Asp Asp Thr
    2315                  2320                  2325


Tyr Gly   Pro Tyr Ser Ser Pro   Ser Leu Arg Ile Ala   Arg Phe Arg
    2330                  2335                  2340


Phe Arg   Ala Phe His Phe Leu   Asn Arg Phe Pro Ser   Val Tyr Leu
    2345                  2350                  2355


Arg Cys   Lys Met Val Val Cys   Arg Ala Tyr Asp Pro   Ser Ser Arg
    2360                  2365                  2370


Cys Tyr   Arg Gly Cys Val Leu   Arg Ser Lys Arg Asp   Val Gly Ser
    2375                  2380                  2385


Tyr Gln   Glu Lys Val Asp Val   Val Leu Gly Pro Ile   Gln Leu Gln
    2390                  2395                  2400


Thr Pro   Pro Arg Arg Glu Glu   Glu Pro Arg
    2405                  2410


<210>  2617
<211>  143
<212>  PRT
<213>  Homo sapiens

<400>  2617

Met Gly Lys Cys Arg Gly Leu Arg Thr Ala Arg Lys Leu Arg Ser His
1                 5                  10                 15


Arg Arg Asp Gln Lys Trp His Asp Lys Gln Tyr Lys Lys Ala His Leu
            20                  25                  30
```

```
Gly Thr Ala Leu Lys Ala Asn Pro Phe Gly Gly Ala Ser His Ala Lys
        35                  40                  45


Gly Ile Val Leu Glu Lys Val Gly Val Glu Ala Lys Gln Pro Asn Ser
    50                  55                  60


Ala Ile Arg Lys Cys Val Arg Val Gln Leu Ile Lys Asn Gly Lys Lys
65                  70                  75                  80


Ile Thr Ala Phe Val Pro Asn Asp Gly Cys Leu Asn Phe Ile Glu Glu
            85                  90                  95            .


Asn Asp Glu Val Leu Val Ala Gly Phe Gly Arg Lys Gly His Ala Val
            100                 105                 110


Gly Asp Ile Pro Gly Val Arg Phe Lys Val Val Lys Val Ala Asn Val
        115                 120                 125


Ser Leu Leu Ala Leu Tyr Lys Gly Lys Lys Glu Arg Pro Arg Ser
    130                 135                 140
```

```
<210>   2618
<211>   272
<212>   PRT
<213>   Homo sapiens

<400>   2618

Met Glu Glu Glu Ala Ile Ala Ser Leu Pro Gly Glu Glu Thr Glu Asp
1               5                   10                  15


Met Asp Phe Leu Ser Gly Leu Glu Leu Ala Asp Leu Leu Asp Pro Arg
            20                  25                  30


Gln Pro Asp Trp His Leu Asp Pro Gly Leu Ser Ser Pro Gly Pro Leu
        35                  40                  45


Ser Ser Ser Gly Gly Gly Ser Asp Ser Gly Gly Leu Trp Arg Gly Asp
    50                  55                  60


Asp Asp Asp Glu Ala Ala Ala Ala Glu Met Gln Arg Phe Ser Asp Leu
65                  70                  75                  80


Leu Gln Arg Leu Leu Asn Gly Ile Gly Gly Cys Ser Ser Ser Ser Asp
            85                  90                  95  .
```

```
    Ser Gly Ser Ala Glu Lys Arg Arg Arg Lys Ser Pro Gly Gly Gly Gly
            100                 105             110


    Gly Gly Gly Ser Gly Asn Asp Asn Asn Gln Ala Ala Thr Lys Ser Pro
            115                 120             125


    Arg Lys Ala Ala Ala Ala Ala Ala Arg Leu Asn Arg Leu Lys Lys Lys
        130                 135             140


    Glu Tyr Val Met Gly Leu Glu Ser Arg Val Arg Gly Leu Ala Ala Glu
    145                 150             155                 160


    Asn Gln Glu Leu Arg Ala Glu Asn Arg Glu Leu Gly Lys Arg Val Gln
                165                 170             175


    Ala Leu Gln Glu Glu Ser Arg Tyr Leu Arg Ala Val Leu Ala Asn Glu
                180                 185             190


    Thr Gly Leu Ala Arg Leu Leu Ser Arg Leu Ser Gly Val Gly Leu Arg
            195                 200             205


    Leu Thr Thr Ser Leu Phe Arg Asp Ser Pro Ala Gly Asp His Asp Tyr
        210                 215             220


    Ala Leu Pro Val Gly Lys Gln Lys Gln Asp Leu Leu Glu Glu Asp Asp
    225                 230             235                 240


    Ser Ala Gly Gly Val Cys Leu His Val Asp Lys Asp Lys Val Ser Val
                245                 250             255


    Glu Phe Cys Ser Ala Cys Ala Arg Lys Ala Ser Ser Ser Leu Lys Met
                260                 265             270
```

<210> 2619
<211> 694
<212> PRT
<213> Homo sapiens

<400> 2619

```
    Met Lys His Leu Lys Arg Trp Trp Ser Ala Gly Gly Gly Leu Leu His
    1               5                   10                  15


    Leu Thr Leu Leu Leu Ser Leu Ala Gly Leu Arg Val Asp Leu Asp Leu
                20                  25                  30


    Tyr Leu Leu Leu Pro Pro Pro Thr Leu Leu Gln Asp Glu Leu Leu Phe
            35                  40                  45
```

```
Leu Gly Gly Pro Ala Ser Ser Ala Tyr Ala Leu Ser Pro Phe Ser Ala
    50              55              60

Ser Gly Gly Trp Gly Arg Ala Gly His Leu His Pro Lys Gly Arg Glu
65              70              75                      80

Leu Asp Pro Ala Ala Pro Pro Glu Gly Gln Leu Leu Arg Glu Val Arg
            85              90                      95

Ala Leu Gly Val Pro Phe Val Pro Arg Thr Ser Val Asp Ala Trp Leu
            100             105             110

Val His Ser Val Ala Ala Gly Ser Ala Asp Glu Ala His Gly Leu Leu
        115             120             125

Gly Ala Ala Ala Ala Ser Ser Thr Gly Gly Ala Gly Ala Ser Val Asp
    130             135             140

Gly Gly Ser Gln Ala Val Gln Gly Gly Gly Gly Asp Pro Arg Ala Ala
145             150             155             160

Arg Ser Gly Pro Leu Asp Ala Gly Glu Glu Glu Lys Ala Pro Ala Glu
            165             170             175

Pro Thr Ala Gln Val Pro Asp Ala Gly Gly Cys Ala Ser Glu Glu Asn
            180             185             190

Gly Val Leu Arg Glu Lys His Glu Ala Val Asp His Ser Ser Gln His
    195             200             205

Glu Glu Asn Glu Glu Arg Val Ser Ala Gln Lys Glu Asn Ser Leu Gln
    210             215             220

Gln Asn Asp Asp Asp Glu Asn Lys Ile Ala Glu Lys Pro Asp Trp Glu
225             230             235             240

Ala Glu Lys Thr Thr Glu Ser Arg Asn Glu Arg His Leu Asn Gly Thr
            245             250             255

Asp Thr Ser Phe Ser Leu Glu Asp Leu Phe Gln Leu Leu Ser Ser Gln
            260             265             270

Pro Glu Asn Ser Leu Glu Gly Ile Ser Leu Gly Asp Ile Pro Leu Pro
    275             280             285
```

```
Gly Ser Ile Ser Asp Gly Met Asn Ser Ser Ala His Tyr His Val Asn
    290             295             300

Phe Ser Gln Ala Ile Ser Gln Asp Val Asn Leu His Glu Ala Ile Leu
305             310             315             320

Leu Cys Pro Asn Asn Thr Phe Arg Arg Asp Pro Thr Ala Arg Thr Ser
            325             330             335

Gln Ser Gln Glu Pro Phe Leu Gln Leu Asn Ser His Thr Thr Asn Pro
        340             345             350

Glu Gln Thr Leu Pro Gly Thr Asn Leu Thr Gly Phe Leu Ser Pro Val
        355             360             365

Asp Asn His Met Arg Asn Leu Thr Ser Gln Asp Leu Leu Tyr Asp Leu
    370             375             380

Asp Ile Asn Ile Phe Asp Glu Ile Asn Leu Met Ser Leu Ala Thr Glu
385.            390             395             400

Asp Asn Phe Asp Pro Ile Asp Val Ser Gln Leu Phe Asp Glu Pro Asp
            405             410             415

Ser Asp Ser Gly Leu Ser Leu Asp Ser Ser His Asn Asn Thr Ser Val
            420             425             430

Ile Lys Ser Asn Ser Ser His Ser Val Cys Asp Glu Gly Ala Ile Gly
        435             440             445

Tyr Cys Thr Asp His Glu Ser Ser Ser His His Asp Leu Glu Gly Ala
    450             455             460

Val Gly Gly Tyr Tyr Pro Glu Pro Ser Lys Leu Cys His Leu Asp Gln
465             470             475             480

Ser Asp Ser Asp Phe His Gly Asp Leu Thr Phe Gln His Val Phe His
            485             490             495

Asn His Thr Tyr His Leu Gln Pro Thr Ala Pro Glu Ser Thr Ser Glu
            500             505             510

Pro Phe Pro Trp Pro Gly Lys Ser Gln Lys Ile Arg Ser Arg Tyr Leu
        515             520             525
```

```
Glu Asp Thr Asp Arg Asn Leu Ser Arg Asp Glu Gln Arg Ala Lys Ala
    530             535             540

Leu His Ile Pro Phe Ser Val Asp Glu Ile Val Gly Met Pro Val Asp
545             550             555             560

Ser Phe Asn Ser Met Leu Ser Arg Tyr Tyr Leu Thr Asp Leu Gln Val
                565             570             575

Ser Leu Ile Arg Asp Ile Arg Arg Arg Gly Lys Asn Lys Val Ala Ala
            580             585             590

Gln Asn Cys Arg Lys Arg Lys Leu Asp Ile Ile Leu Asn Leu Glu Asp
    595             600             605

Asp Val Cys Asn Leu Gln Ala Lys Lys Glu Thr Leu Lys Arg Glu Gln
    610             615             620

Ala Gln Cys Asn Lys Ala Ile Asn Ile Met Lys Gln Lys Leu His Asp
625             630             635             640

Leu Tyr His Asp Ile Phe Ser Arg Leu Arg Asp Asp Gln Gly Arg Pro
            645             650             655

Val Asn Pro Asn His Tyr Ala Leu Gln Cys Thr His Asp Gly Ser Ile
            660             665             670

Leu Ile Val Pro Lys Glu Leu Val Ala Ser Gly His Lys Lys Glu Thr
            675             680             685

Gln Lys Gly Lys Arg Lys
    690
```

```
<210>  2620
<211>  391
<212>  PRT
<213>  Homo sapiens

<400>  2620

Met Lys Cys Leu Val Thr Gly Gly Asn Val Lys Val Leu Gly Lys Ala
1               5               10              15

Val His Ser Leu Ser Arg Ile Gly Asp Glu Leu Tyr Leu Glu Pro Leu
            20              25              30

Glu Asp Gly Leu Ser Leu Arg Thr Val Asn Ser Ser Arg Ser Ala Tyr
            35              40              45
```

Ala Cys Phe Leu Phe Ala Pro Leu Phe Phe Gln Gln Tyr Gln Ala Ala
    50   55   60

Thr Pro Gly Gln Asp Leu Leu Arg Cys Lys Ile Leu Met Lys Ser Phe
65   70   75   80

Leu Ser Val Phe Arg Ser Leu Ala Met Leu Glu Lys Thr Val Glu Lys
                85   90   95

Cys Cys Ile Ser Leu Asn Gly Arg Ser Ser Arg Leu Val Val Gln Leu
            100   105   110

His Cys Lys Phe Gly Val Arg Lys Thr His Asn Leu Ser Phe Gln Asp
        115   120   125

Cys Glu Ser Leu Gln Ala Val Phe Asp Pro Ala Ser Cys Pro His Met
    130   135   140

Leu Arg Ala Pro Ala Arg Val Leu Gly Glu Ala Val Leu Pro Phe Ser
145   150   155   160

Pro Ala Leu Ala Glu Val Thr Leu Gly Ile Gly Arg Gly Arg Arg Val
                165   170   175

Ile Leu Arg Ser Tyr His Glu Glu Glu Ala Asp Ser Thr Ala Lys Ala
            180   185   190

Met Val Thr Glu Met Cys Leu Gly Glu Glu Asp Phe Gln Gln Leu Gln
        195   200   205

Ala Gln Glu Gly Val Ala Ile Thr Phe Cys Leu Lys Glu Phe Arg Gly
    210   215   220

Leu Leu Ser Phe Ala Glu Ser Ala Asn Leu Asn Leu Ser Ile His Phe
225   230   235   240

Asp Ala Pro Gly Arg Pro Ala Ile Phe Thr Ile Lys Asp Ser Leu Leu
                245   250   255

Asp Gly His Phe Val Leu Ala Thr Leu Ser Asp Thr Asp Ser His Ser
            260   265   270

Gln Asp Leu Gly Ser Pro Glu Arg His Gln Pro Val Pro Gln Leu Gln
        275   280   285

```
Ala His Ser Thr Pro His Pro Asp Asp Phe Ala Asn Asp Asp Ile Asp
    290             295             300
```

```
Ser Tyr Met Ile Ala Met Glu Thr Thr Ile Gly Asn Glu Gly Ser Arg
305             310             315             320
```

```
Val Leu Pro Ser Ile Ser Leu Ser Pro Gly Pro Gln Pro Pro Lys Ser
            325             330             335
```

```
Pro Gly Pro His Ser Glu Glu Glu Asp Glu Ala Glu Pro Ser Thr Val
            340             345             350
```

```
Pro Gly Thr Pro Pro Pro Lys Lys Phe Arg Ser Leu Phe Phe Gly Ser
        355             360             365
```

```
Ile Leu Ala Pro Val Arg Ser Pro Gln Gly Pro Ser Pro Val Leu Ala
    370             375             380
```

```
Glu Asp Ser Glu Gly Glu Gly
385             390
```

```
<210>   2621
<211>   1429
<212>   PRT
<213>   Homo sapiens
```

```
<400>   2621
```

```
Met Ala Gly Gly Ala Trp Gly Arg Leu Ala Cys Tyr Leu Glu Phe Leu
1               5               10              15
```

```
Lys Lys Glu Glu Leu Lys Glu Phe Gln Leu Leu Leu Ala Asn Lys Ala
            20              25              30
```

```
His Ser Arg Ser Ser Ser Gly Glu Thr Pro Ala Gln Pro Glu Lys Thr
        35              40              45
```

```
Ser Gly Met Glu Val Ala Ser Tyr Leu Val Ala Gln Tyr Gly Glu Gln
    50              55              60
```

```
Arg Ala Trp Asp Leu Ala Leu His Thr Trp Glu Gln Met Gly Leu Arg
65              70              75              80
```

```
Ser Leu Cys Ala Gln Ala Gln Glu Gly Ala Gly His Ser Pro Ser Phe
                85              90              95
```

```
Pro Tyr Ser Pro Ser Glu Pro His Leu Gly Ser Pro Ser Gln Pro Thr
```

                    100   105   110

        Ser Thr Ala Val Leu Met Pro Trp Ile His Glu Leu Pro Ala Gly Cys
            115   120   125

        Thr Gln Gly Ser Glu Arg Arg Val Leu Arg Gln Leu Pro Asp Thr Ser
            130   135   140

        Gly Arg Arg Trp Arg Glu Ile Ser Ala Ser Leu Leu Tyr Gln Ala Leu
        145   150   155   160

        Pro Ser Ser Pro Asp His Glu Ser Pro Ser Gln Glu Ser Pro Asn Ala
                        165   170   175

        Pro Thr Ser Thr Ala Val Leu Gly Ser Trp Gly Ser Pro Pro Gln Pro
                        180   185   190

        Ser Leu Ala Pro Arg Glu Gln Glu Ala Pro Gly Thr Gln Trp Pro Leu
            195   200   205

        Asp Glu Thr Ser Gly Ile Tyr Tyr Thr Glu Ile Arg Glu Arg Glu Arg
            210   215   220

        Glu Lys Ser Glu Lys Gly Arg Pro Pro Trp Ala Ala Val Val Gly Thr
        225   230   235   240

        Pro Pro Gln Ala His Thr Ser Leu Gln Pro His His His Pro Trp Glu
                        245   250   255

        Pro Ser Val Arg Glu Ser Leu Cys Ser Thr Trp Pro Trp Lys Asn Glu
                        260   265   270

        Asp Phe Asn Gln Lys Phe Thr Gln Leu Leu Leu Leu Gln Arg Pro His
                        275   280   285

    ·   Pro Arg Ser Gln Asp Pro Leu Val Lys Arg Ser Trp Pro Asp Tyr Val
            290   295   300

    ⁻   Glu Glu Asn Arg Gly His Leu Ile Glu Ile Arg Asp Leu Phe Gly Pro
        305   310   315   320

        Gly Leu Asp Thr Gln Glu Pro Arg Ile Val Ile Leu Gln Gly Ala Ala
                        325   330   335

        Gly Ile Gly Lys Ser Thr Leu Ala Arg Gln Val Lys Glu Ala Trp Gly
                        340   345   350

```
Arg Gly Gln Leu Tyr Gly Asp Arg Phe Gln His Val Phe Tyr Phe Ser
        355             360             365

Cys Arg Glu Leu Ala Gln Ser Lys Val Val Ser Leu Ala Glu Leu Ile
    370             375             380

Gly Lys Asp Gly Thr Ala Thr Pro Ala Pro Ile Arg Gln Ile Leu Ser
385             390             395             400

Arg Pro Glu Arg Leu Leu Phe Ile Leu Asp Gly Val Asp Glu Pro Gly
            405             410             415

Trp Val Leu Gln Glu Pro Ser Ser Glu Leu Cys Leu His Trp Ser Gln
        420             425             430

Pro Gln Pro Ala Asp Ala Leu Leu Gly Ser Leu Leu Gly Lys Thr Ile
    435             440             445

Leu Pro Glu Ala Ser Phe Leu Ile Thr Ala Arg Thr Thr Ala Leu Gln
    450             455             460

Asn Leu Ile Pro Ser Leu Glu Gln Ala Arg Trp Val Glu Val Leu Gly
465             470             475             480

Phe Ser Glu Ser Ser Arg Lys Glu Tyr Phe Tyr Arg Tyr Phe Thr Asp
            485             490             495

Glu Arg Gln Ala Ile Arg Ala Phe Arg Leu Val Lys Ser Asn Lys Glu
            500             505             510

Leu Trp Ala Leu Cys Leu Val Pro Trp Val Ser Trp Leu Ala Cys Thr
        515             520             525

Cys Leu Met Gln Gln Met Lys Arg Lys Glu Lys Leu Thr Leu Thr Ser
    530             535             540

Lys Thr Thr Thr Thr Leu Cys Leu His Tyr Leu Ala Gln Ala Leu Gln
545             550             555             560

Ala Gln Pro Leu Gly Pro Gln Leu Arg Asp Leu Cys Ser Leu Ala Ala
            565             570             575

Glu Gly Ile Trp Gln Lys Lys Thr Leu Phe Ser Pro Asp Asp Leu Arg
            580             585             590
```

Lys His Gly Leu Asp Gly Ala Ile Ile Ser Thr Phe Leu Lys Met Gly
        595   600   605

Ile Leu Gln Glu His Pro Ile Pro Leu Ser Tyr Ser Phe Ile His Leu
    610   615   620

Cys Phe Gln Glu Phe Phe Ala Ala Met Ser Tyr Val Leu Glu Asp Glu
625   630   .   635   640

Lys Gly Arg Gly Lys His Ser Asn Cys Ile Ile Asp Leu Glu Lys Thr
                645   650   655

Leu Glu Ala Tyr Gly Ile His Gly Leu Phe Gly Ala Ser Thr Thr Arg
            660   665   670

Phe Leu Leu Gly Leu Leu Ser Asp Glu Gly Glu Arg Glu Met Glu Asn
        675   680   685

Ile Phe His Cys Arg Leu Ser Gln Gly Arg Asn Leu Met Gln Trp Val
    690   695   700

Pro Ser Leu Gln Leu Leu Leu Gln Pro His Ser Leu Glu Ser Leu His
705   710   715   720

Cys Leu Tyr Glu Thr Arg Asn Lys Thr Phe Leu Thr Gln Val Met Ala
            725   730   735

His Phe Glu Glu Met Gly Met Cys Val Glu Thr Asp Met Glu Leu Leu
            740   745   750

Val Cys Thr Phe Cys Ile Lys Phe Ser Arg His Val Lys Lys Leu Gln
            755   760   765

Leu Ile Glu Gly Arg Gln His Arg Ser Thr Trp Ser Pro Thr Met Val
    770   775   780

Val Leu Phe Arg Trp Val Pro Val Thr Asp Ala Tyr Trp Gln Ile Leu
785   790   795   800

Phe Ser Val Leu Lys Val Thr Arg Asn Leu Lys Glu Leu Asp Leu Ser
                805   810   815

Gly Asn Ser Leu Ser His Ser Ala Val Lys Ser Leu Cys Lys Thr Leu
                820   825   830

Arg Arg Pro Arg Cys Leu Leu Glu Thr Leu Arg Leu Ala Gly Cys Gly
        835   840   845

Leu Thr Ala Glu Asp Cys Lys Asp Leu Ala Phe Gly Leu Arg Ala Asn
    850   855   860

Gln Thr Leu Thr Glu Leu Asp Leu Ser Phe Asn Val Leu Thr Asp Ala
865   870   875   880

Gly Ala Lys His Leu Cys Gln Arg Leu Arg Gln Pro Ser Cys Lys Leu
            885   890   895

Gln Arg Leu Gln Leu Val Ser Cys Gly Leu Thr Ser Asp Cys Cys Gln
        900   905   910

Asp Leu Ala Ser Val Leu Ser Ala Ser Pro Ser Leu Lys Glu Leu Asp
        915   920   925

Leu Gln Gln Asn Asn Leu Asp Asp Val Gly Val Arg Leu Leu Cys Glu
    930   935   940

Gly Leu Arg His Pro Ala Cys Lys Leu Ile Arg Leu Gly Leu Asp Gln
945   950   955   960

Thr Thr Leu Ser Asp Glu Met Arg Gln Glu Leu Arg Ala Leu Glu Gln
            965   970   975

Glu Lys Pro Gln Leu Leu Ile Phe Ser Arg Arg Lys Pro Ser Val Met
        980   985   990

Thr Pro Thr Glu Gly Leu Asp Thr Gly Glu Met Ser Asn Ser Thr Ser
        995   1000   1005

Ser Leu Lys Arg Gln Arg Leu Gly Ser Glu Arg Ala Ala Ser His
    1010   1015   1020

Val Ala Gln Ala Asn Leu Lys Leu Leu Asp Val Ser Lys Ile Phe
    1025   1030   1035

Pro Ile Ala Glu Ile Ala Glu Glu Ser Ser Pro Glu Val Val Pro
    1040   1045   1050

Val Glu Leu Leu Cys Val Pro Ser Pro Ala Ser Gln Gly Asp Leu
    1055   1060   1065

His Thr Lys Pro Leu Gly Thr Asp Asp Asp Phe Trp Gly Pro Thr

```
        1070                    1075                    1080


    Gly Pro  Val Ala Thr Glu Val  Val Asp Lys Glu Lys  Asn Leu Tyr
         1085                1090                1095


    Arg Val  His Phe Pro Val Ala  Gly Ser Tyr Arg Trp  Pro Asn Thr
         1100                1105                1110
      .

    Gly Leu  Cys Phe Val Met Arg  Glu Ala Val Thr Val  Glu Ile Glu
         1115                1120                1125    .


    Phe Cys  Val Trp Asp Gln Phe  Leu Gly Glu Ile Asn  Pro Gln His
         1130                1135                1140


    Ser Trp  Met Val Ala Gly Pro  Leu Leu Asp Ile Lys  Ala Glu Pro
         1145                1150                1155


    Gly Ala  Val Glu Ala Val His  Leu Pro His Phe Val  Ala Leu Gln
         1160                1165                ·1170


    Gly Gly  His Val Asp Thr Ser  Leu Phe Gln Met Ala  His Phe Lys
         1175                1180                1185


    Glu Glu  Gly Met Leu Leu Glu  Lys Pro Ala Arg Val  Glu Leu His
         1190                1195                1200


    His Ile  Val Leu Glu Asn Pro  Ser Phe Ser Pro Leu  Gly Val Leu
         1205                1210                1215


    Leu Lys  Met Ile His Asn Ala  Leu Arg Phe Ile Pro  Val Thr Ser
         1220                1225                1230    .


    Val Val  Leu Leu Tyr His Arg  Val His Pro Glu Glu  Val Thr Phe
         1235                1240                1245


    His Leu  Tyr Leu Ile Pro Ser  Asp Cys Ser Ile Arg  Lys Glu Leu
         1250                1255                1260


    Glu Leu  Cys Tyr Arg Ser Pro  Gly Glu Asp Gln Leu  Phe Ser Glu
         1265                1270                1275


    Phe Tyr  Val Gly His Leu Gly  Ser Gly Ile Arg Leu  Gln Val Lys
         1280                1285                1290


    Asp Lys  Lys Asp Glu Thr Leu  Val Trp Glu Ala Leu  Val Lys Pro .
         1295                1300                1305
```

```
Gly Asp Leu Met Pro Ala Thr  Thr Leu Ile Pro Pro  Ala Arg Ile
    1310                1315              1320

Ala Val Pro Ser Pro Leu Asp  Ala Pro Gln Leu Leu  His Phe Val
    1325                1330              1335

Asp Gln Tyr Arg Glu Gln Leu  Ile Ala Arg Val Thr  Ser Val Glu
    1340                1345              1350

Val Val Leu Asp Lys Leu His  Gly Gln Val Leu Ser  Gln Glu Gln
    1355                1360              1365

Tyr Glu Arg Val Leu Ala Glu  Asn Thr Arg Pro Ser  Gln Met Arg
    1370                1375              1380

Lys Leu Phe Ser Leu Ser Gln  Ser Trp Asp Arg Lys  Cys Lys Asp
    1385                1390              1395

Gly Leu Tyr Gln Ala Leu Lys  Glu Thr His Pro His  Leu Ile Met
    1400                1405              1410

Glu Leu Trp Glu Lys Gly Ser  Lys Lys Gly Leu Leu  Pro Leu Ser
    1415                1420              1425

Ser
```

```
<210>  2622
<211>  179
<212>  PRT
<213>  Homo sapiens

<400>  2622

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
1              5               10                  15

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
            20              25                  30

Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln
        35              40                  45

Gln Pro Tyr Ile Thr Asn Arg Thr Phe Met Leu Ala Lys Glu Ala Ser
    50              55                  60
```

```
Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe
65                  70              75                  80


His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu
                85              90                  95


Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln
            100             105             110


Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg
            115             120             125


Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn
        130             135             140


Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu
145             150             155             160


Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn
            165             170             175


Ala Cys Ile



<210>  2623
<211>  261
<212>  PRT
<213>  Homo sapiens

<400>  2623

Met Ser Arg Arg Tyr Asp Ser Arg Thr Thr Ile Phe Ser Pro Glu Gly
1               5               10              15


Arg Leu Tyr Gln Val Glu Tyr Ala Met Glu Ala Ile Gly His Ala Gly
            20              25              30


Thr Cys Leu Gly Ile Leu Ala Asn Asp Gly Val Leu Leu Ala Ala Glu
        35              40              45


Arg Arg Asn Ile His Lys Leu Leu Asp Glu Val Phe Phe Ser Glu Lys
    50              55              60


Ile Tyr Lys Leu Asn Glu Asp Met Ala Cys Ser Val Ala Gly Ile Thr
65              70              75              80


Ser Asp Ala Asn Val Leu Thr Asn Glu Leu Arg Leu Ile Ala Gln Arg
            85              90              95
```

Tyr Leu Leu Gln Tyr Gln Glu Pro Ile Pro Cys Glu Gln Leu Val Thr
            100   105   110

Ala Leu Cys Asp Ile Lys Gln Ala Tyr Thr Gln Phe Gly Gly Lys Arg
            115   120   125

Pro Phe Gly Val Ser Leu Leu Tyr Ile Gly Trp Asp Lys His Tyr Gly
    130   135   140

Phe Gln Leu Tyr Gln Ser Asp Pro Ser Gly Asn Tyr Gly Gly Trp Lys
145   150   155   160

Ala Thr Cys Ile Gly Asn Asn Ser Ala Ala Ala Val Ser Met Leu Lys
                165   170   175

Gln Asp Tyr Lys Glu Gly Glu Met Thr Leu Lys Ser Ala Leu Ala Leu
            180   185   190

Ala Ile Lys Val Leu Asn Lys Thr Met Asp Val Ser Lys Leu Ser Ala
            195   200   205

Glu Lys Val Glu Ile Ala Thr Leu Thr Arg Glu Asn Gly Lys Thr Val
    210   215   220

Ile Arg Val Leu Lys Gln Lys Glu Val Glu Gln Leu Ile Lys Lys His
225   230   235   240

Glu Glu Glu Glu Ala Lys Ala Glu Arg Glu Lys Lys Glu Lys Glu Gln
                245   250   255

Lys Glu Lys Asp Lys
            260

<210> 2624
<211> 377
<212> PRT
<213> Homo sapiens

<400> 2624

Met Lys Phe Pro Gly Pro Leu Glu Asn Gln Arg Leu Ser Phe Leu Leu
1   5   10   15

Glu Lys Ala Ile Thr Arg Glu Ala Gln Met Trp Lys Val Asn Val Arg
            20   25   30

```
     Lys Met Pro Ser Asn Gln Asn Val Ser Pro Ser Gln Arg Asp Glu Val
             35                  40                  45


     Ile Gln Trp Leu Ala Lys Leu Lys Tyr Gln Phe Asn Leu Tyr Pro Glu
             50                  55                  60


     Thr Phe Ala Leu Ala Ser Ser Leu Leu Asp Arg Phe Leu Ala Thr Val
     65                  70                  75                  80


     Lys Ala His Pro Lys Tyr Leu Ser Cys Ile Ala Ile Ser Cys Phe Phe
                     85                  90                  95


     Leu Ala Ala Lys Thr Val Glu Glu Asp Glu Arg Ile Pro Val Leu Lys
                     100                 105                 110


     Val Leu Ala Arg Asp Ser Phe Cys Gly Cys Ser Ser Ser Glu Ile Leu
                 115                 120                 125


     Arg Met Glu Arg Ile Ile Leu Asp Lys Leu Asn Trp Asp Leu His Thr
         130                 135                 140


     Ala Thr Pro Leu Asp Phe Leu His Ile Phe His Ala Ile Ala Val Ser
     145                 150                 155                 160


     Thr Arg Pro Gln Leu Leu Phe Ser Leu Pro Lys Leu Ser Pro Ser Gln
                 165                 170                 175


     His Leu Ala Val Leu Thr Lys Gln Leu Leu His Cys Met Ala Cys Asn
                 180                 185                 190


     Gln Leu Leu Gln Phe Arg Gly Ser Met Leu Ala Leu Ala Met Val Ser
             195                 200                 205


     Leu Glu Met Glu Lys Leu Ile Pro Asp Trp Leu Ser Leu Thr Ile Glu
         210                 215                 220


     Leu Leu Gln Lys Ala Gln Met Asp Ser Ser Gln Leu Ile His Cys Arg
     225                 230                 235                 240


     Glu Leu Val Ala His His Leu Ser Thr Leu Gln Ser Ser Leu Pro Leu
                 245                 250                 255


     Asn Ser Val Tyr Val Tyr Arg Pro Leu Lys His Thr Leu Val Thr Cys
                 260                 265                 270


     Asp Lys Gly Val Phe Arg Leu His Pro Ser Ser Val Pro Gly Pro Asp
```

                275   280   285

Phe Ser Lys Asp Asn Ser Lys Pro Glu Val Pro Val Arg Gly Thr Ala
    290   295   300

Ala Phe Tyr His His Leu Pro Ala Ala Ser Gly Cys Lys Gln Thr Ser
305   310   315   320

Thr Lys Arg Lys Val Glu Glu Met Glu Val Asp Asp Phe Tyr Asp Gly
                325   330   335

Ile Lys Arg Leu Tyr Asn Glu Asp Asn Val Ser Glu Asn Val Gly Ser
            340   345   350

Val Cys Gly Thr Asp Leu Ser Arg Gln Glu Gly His Ala Ser Pro Cys
            355   360   365

Pro Pro Leu Gln Pro Val Ser Val Met
    370   375

<210> 2625
<211> 575
<212> PRT
<213> Homo sapiens

<400> 2625

Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly
1   5   10   15

Phe Pro Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu
            20   25   30

His Asp Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala
        35   40   45

Ser Gln Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser
    50   55   60

Ser Val Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly
65   70   75   80

Val Gly Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys
                85   90   95

Gly Asp Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr
            100   105   110

Gly Asp Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn
        115   120   125

Gly Ala Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu
        130   135   140

Ala Thr Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val
145   150   155   160

Lys Ala Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg
                165   170   175

Pro Leu Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr
                180   185   190

Tyr Gly Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro
        195   200   205

Val Gly Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys
210   215   220

Thr Ala Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro
225   230   235   240

Gly Ala Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys
                245   250   255

Asn Ala Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala
                260   265   270

Leu Gln Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys
        275   280   285

Asn Asp Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly
        290   295   300

Ser Tyr Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln
305   310   315   320

His Arg Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys
                325   330   335

Pro Gln Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr
        340   345   350

```
Pro Asn Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro
        355             360             365


Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr
    370             375             380


Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu
385             390             395             400


Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp
            405             410             415


Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile
            420             425             430


Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly
        435             440             445


Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys
    450             455             460


Ile Cys Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys
465             470             475             480


Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro
            485             490             495


Pro Ser Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu
            500             505             510


Val His Ser Gly Leu Leu Ile Gly Ile Ser Ile Ala Ser Leu Cys Leu
    515             520             525


Val Val Ala Leu Leu Ala Leu Leu Cys His Leu Arg Lys Lys Gln Gly
    530             535             540


Ala Ala Arg Ala Lys Met Glu Tyr Lys Cys Ala Ala Pro Ser Lys Glu
545             550             555             560


Val Val Leu Gln His Val Arg Thr Glu Arg Thr Pro Gln Arg Leu
            565             570             575


<210>  2626
<211>  332
<212>  PRT
<213>  Homo sapiens
```

<400> 2626

Met Ala Ala Val Phe Leu Val Thr Leu Tyr Glu Tyr Ser Pro Leu Phe
1   5   10   15

Tyr Ile Ala Val Val Phe Thr Cys Phe Ile Val Thr Thr Gly Leu Val
        20   25   30

Leu Gly Trp Phe Gly Trp Asp Val Pro Val Ile Leu Arg Asn Ser Glu
        35   40   45

Glu Thr Gln Phe Ser Thr Arg Val Phe Lys Lys Gln Met Arg Gln Val
    50   55   60

Lys Asn Pro Phe Gly Leu Glu Ile Thr Asn Pro Ser Ser Ala Ser Ile
65   70   75   80

Thr Thr Gly Ile Thr Leu Thr Thr Asp Cys Leu Glu Asp Ser Leu Leu
            85   90   95

Thr Cys Tyr Trp Gly Cys Ser Val Gln Lys Leu Tyr Glu Ala Leu Gln
        100   105   110

Lys His Val Tyr Cys Phe Arg Ile Ser Thr Pro Gln Ala Leu Glu Asp
        115   120   125

Ala Leu Tyr Ser Glu Tyr Leu Tyr Gln Glu Gln Tyr Phe Ile Lys Lys
    130   135   140

Asp Ser Lys Glu Glu Ile Tyr Cys Gln Leu Pro Arg Asp Thr Lys Ile
145   150   155   160

Glu Asp Phe Gly Thr Val Pro Arg Ser Arg Tyr Pro Leu Val Ala Leu
            165   170   175

Leu Thr Leu Ala Asp Glu Asp Asp Arg Glu Ile Tyr Asp Ile Ile Ser
        180   185   190

Met Val Ser Val Ile His Ile Pro Asp Arg Thr Tyr Lys Leu Ser Cys
        195   200   205

Arg Ile Leu Tyr Gln Tyr Leu Leu Leu Ala Gln Gly Gln Phe His Asp
    210   215   220

Leu Lys Gln Leu Phe Met Ser Ala Asn Asn Asn Phe Thr Pro Ser Asn
225   230   235   240

```
Asn Ser Ser Ser Glu Glu Lys Asn Thr Asp Arg Ser Leu Leu Glu Lys
            245                 250                 255
```

```
Val Gly Leu Ser Glu Ser Glu Val Glu Pro Ser Glu Glu Asn Ser Lys
            260                 265                 270
```

```
Asp Cys Val Val Cys Gln Asn Gly Thr Val Asn Trp Val Leu Leu Pro
            275                 280                 285
```

```
Cys Arg His Thr Cys Leu Cys Asp Gly Cys Val Lys Tyr Phe Gln Gln
    290                 295                 300
```

```
Cys Pro Met Cys Arg Gln Phe Val Gln Glu Ser Phe Ala Leu Cys Ser
305                 310                 315                 320
```

```
Gln Lys Glu Gln Asp Lys Asp Lys Pro Lys Thr Leu
            325                 330
```

```
<210>  2627
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  2627
agagcacttg cagagcctgg gacaacctcc ttattgaagg gaagagggac          50


<210>  2628
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  2628
taaggagtgt tggagatatg tgatttggct agtgctattt aaagacaccc          50


<210>  2629
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  2629
gccaagacaa taagctaggc tactgggtcc agctactact ttggtgggat          50


<210>  2630
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  2630
gtaaaggcta tacttgtctt gttcaccttg ggatgacgcc gcatgatatg          50
```

```
<210>   2631
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2631
tgtcagagat tgcctgtggc tctaatatgc acctcaagat tttaaggaga          50


<210>   2632
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2632
ctttgcctaa accctatggc ctcctgtgca tctgtactca ccctgtacca          50


<210>   2633
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2633
accttgggtt gagtaatgct cgtctgtgtg ttttagtttc atcacctgtt          50


<210>   2634
<211>   70
<212>   DNA
<213>   Homo sapiens

<400>   2634
atttatatta gtttagccaa aggataagtg tcctatgggg atggtccact gtcactgttt    60

ctctgctgtt                                                      70


<210>   2635
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2635
cccatgtaag caccccttca tttggcattc cccacttgag aattaccctt          50


<210>   2636
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2636
tggaccgtaa tgaatgaatg tacacgccat aaacgccctt tgttcaagca          50


<210>   2637
<211>   50
<212>   DNA
<213>   Homo sapiens
```

<400> 2637
tttcaagaca gaaagtgacg cagagaacct ccccggccca gtctcgacgc   50

<210> 2638
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2638
tgcactaaac agttgcccca aaagacatat cttgttttaa ggcccagacc   50

<210> 2639
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2639
gggtaggcag cttgcaccca gttctccttt atctcaactt attttcctgg   50

<210> 2640
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2640
ttaatgccag tcctcatgta acctcaggta tcttcagctt gtggagaata   50

<210> 2641
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2641
tgattttgca acttaggatg tttttgagtc ccatggttca ttttgattgt   50

<210> 2642
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2642
tttgagcgat ctctcacatg atggggttct ttagtacatg gtaacagcca   50

<210> 2643
<211> 50
<212> DNA
<213> Homo sapiens

<400> 2643
tgtttcgtaa attaaatagg tctggcccag aagacccact caattgcctt   50

<210> 2644
<211> 50
<212> DNA

<213>   Homo sapiens

<400>   2644
accttgtaag tgcctaagaa atgagactac aagctccatt tcagcaggac   50

<210>   2645
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2645
acagggcctc agcaagggag ccatacattt ttgtaacatt ttgatatgtt   50

<210>   2646
<211>   50
<212>   DNA
<213>   Homo sapiens

<400>   2646
acaaccaacc agtttctttt ctagccaatc atctctgaag agttgctgtt   50

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1120

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attaagaata cacacacacg cacacacaca cacacctgtc tatactagaa tatttaaaag     540

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1123

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1131

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1148

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1149

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<213>    Homo sapiens

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gaggatcgat tctcagctaa gatgcctaat gcatcattct ccactctgaa gatccagccc     180

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gagctgctct cacctctctg catcccaata gatatccccc tatgtgcatg cacacctgca     960

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<213>    Homo sapiens

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cattggcatt gggaccagag accccgcaag tggcctgttt gcctggacat ccacctgtac     180

gtccccaggt ttcgggaggc ccaggggcga tgccagaccc cgcggcgcac ctgcccttct     240
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<213>  Homo sapiens

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aagcctcaag·tgggaggaga aatgcaaatc ccctactgat gatggcgtca gcggctttct    180

cctagggact gtgaggggcg cttctgactt tggacttgag cactgcctgg gacctgtgct    240

gagagagcgc tagcatgtct cagtggaatc aagtccaaca gttagaaatc aagtttttgg    300

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aaacaattca gacaatggat cagagtgaca agaatagtgc catggtgaat caggaagttt    840

tgacactgca ggaaatgctt aacagcctcg atttcaagag aaaggaggct ctcagtaaaa    900

tgacccaaat catccatgag acagacctgt taatgaacac catgctcata gaagagctgc    960

aagactggaa gcggcggcag caaatcgcct gcatcggggg tccactccac aatgggctcg   1020

accagcttca gaactgcttt acactattgg cagaaagtct tttccaactg agaaggcaat   1080

tggagaaact agaggagcaa tctaccaaaa tgacatatga aggtgatccc attccaatgc   1140

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<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

<400> 2820

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1154

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                                      1155

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gta                                                                  3003
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tctttttta aattgtatct aatcctcaac aacaaaccaa aacagaacaa ttaaacagcc    180

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tgattctgaa tctgaaagcc cgcctctgtc ctaaaataca aacaagcaca gacattaaac    480

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1164

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1166

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1171

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atccctggag aatctgctgg aagacccaga aggcgtgaaa agatttaggg aattttaaa      180

aaaggaattc agtgaagaaa atgttttgtt ttggctagca tgtgaagatt ttaagaaaat      240

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cctggcacca tggcccccact gaagatgctg gccctggtca ccctcctcct gggggcttct        180

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tgggaaaatg gctttgtaaa gaagtttgaa cctaaatctg gctggatgac ttttctagaa        660

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caggataaca caagtccctt gccggcgcag ctcgtgtata ctaccaatat ccaggagctc     300

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1181

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1186

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1187

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ttatgtgttg ttttccgttg tgacgaatgt gattggaaca tttggggagc acccagaggg    2580

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aagtttctgg ctttgacgct ctttccaatg gagcacattt tatatgcaac tacggaccag    660

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tcattgttaa ttcagtaatt ctaatactgt ctgttataat taccattttg gtacagctca    900
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1188

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agtaccctaa tttagttctt ttggactaat acaattcagg aaagaaaaaa cccaaaaacc    960

aacctcattc acatatggct tttttttaac caataacaat taggtgtact tctattttaa   1020

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<400> 2844
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gtaagggggg ctttggcacc gtcttcgcag gacaccgcct cacagatcga ctccaggtgg    360

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aaaggaggcc ctgccccttt ggcctggtcc ttgctaccct aagcctggcc tggcctggcc   1140

tggcccccaa tggtcagaag agccatccca tggccatgtc acaggatag atggacattt     1200

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caaaggagcc ttcctcccag aacctgtggt ccctgatttt ggagggggaa cttcttgctt   1380

ctcattttgc taaggaagtt tattttggtg aagttgttcc cattttgagc cccgggactc   1440
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1189

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agtaaaggga ccctttcccc tagcctaggg tcccatattg ggtcaagctg cttacctgcc    1620

tcagcccagg atttttat ttggggggagg taatgccctg ttgttacccc aaggcttctt      1680

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gcttgctgtt tgttttcctg gggcgctccc tccaattttg cagatttttg caacctcctc    1920

ctgagccggg attgtccaat tactaaaatg taaataatca cgtattgtgg ggaggggagt    1980

tccaagtgtg ccctcctttt ttttcctgcc tggattattt aaaaagccat gtgtggaaac    2040

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ggatggtttt ccatactgga acccaaaggt aaagacactc aaggacagac atttttggca    180

gagcatagat gaaaatggca agttccctgg cttttccttct gctcaacttt catgtctccc    240

tcctcttggt ccagctgctc actccttgct cagctcagtt ttctgtgctt ggaccctctg    300

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tgtatgcaga tggaaaggaa gtggaagaca ggcagagtgc accgtatcga gggagaactt    480

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cctctgacag tggaaagtac ttgtgttatt ccaagatgg tgacttctat gaaaaagccc      600

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aggatggagg gatccatctg gagtgcaggt ccaccggctg gtaccccaa ccccaaatac      720

agtggagcaa cgccaaggga gagaacatcc cagctgtgga agcacctgtg gttgcagatg    780

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tggaaaaatg gccctcttca agcctggtga ggaaatgctt cagatgaggc tccaccttgt   1260

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aatcctagca ctttggaagg ctgaggaggg cggatcacaa ggtcaggaga tcaagaccat   1440

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tgaacccgga aggcagagct tgcagtgagc cgagatcacg ccactgcact ccagcctggg   1620

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gcgcttattt ttcttaatca tgtttctgac aatcatagtg tgtggaatgg ttgctgcttt   180

aagcgcaata agagctaact gccatcaaga gccatcagta tgtcttcaag ctgcatgccc   240

agaaagctgg attggttttc aaagaaagtg tttctatttt tctgatgaca ccaagaactg   300

gacatcaagt cagaggtttt gtgactcaca agatgctgat cttgctcagg ttgaaagctt   360

ccaggaactg aatttcctgt tgagatataa aggcccatct gatcactgga ttgggctgag   420

cagagaacaa ggccaaccat ggaaatggat aaatggtact gaatggacaa gacagtttcc   480

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aagccccaac taatctttag aagcatattg gaactgataa ctccatttta aaatgagcaa   660

agaatttatt tcttatacca acaggtatat gaaaatatgc tcaatatcac taataactgg   720

gaaaatacaa atcaaaatca tagtaaaata ttacctgttt tcatggtgct aatattacct   780

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tgctgcagaa attggggaaa gctgtagaaa ccaaagatga acgatttgaa caaagcgcta    180

acaacttcta ccaacaacag gcagaaggcc acaagctgta caaggacctg aagaacttcc    240

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<212> DNA
<213> Homo sapiens

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ggagactcag gagttttgag agcaaaatga caacacccag aaattcagta aatgggactt   180

tcccggcaga gccaatgaaa ggccctattg ctatgcaatc tggtccaaaa ccactcttca   240

ggaggatgtc ttcactggtg ggccccacgc aaagcttctt catgagggaa tctaagactt   300

tgggggctgt ccagattatg aatgggctct tccacattgc cctggggggt cttctgatga   360

tcccagcagg gatctatgca cccatctgtg tgactgtgtg gtaccctctc tggggaggca   420

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ttctttcaat catggacata cttaatatta aaatttccca tttttttaaaa atggagagtc   600

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ttcgatacct cagagcatta ttttcataat gagctgtgtt cacaatcttt ttaggttaac   180

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agagcgactg gctcagccag agcatgttca cctgccgggt ggatcacagg ggcctgacct   1260

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<212>   DNA
<213>   Homo sapiens

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agcagcccct cagcatccag cagcatgagc ggaggcattt tcctttttcttt cgtggccaat    180

gccataatcc acctcttctg cttcagttga ggtgacacgt ctcagcctta gccctgtgcc    240

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atgccagaca tcaccaggtt gtagaagttg acaggcagtg ccatggggggc aacagccaaa    360

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1222

<211> 4882
<212> DNA
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ccactggatt gactacagca aagatgccca gtgttccact ttcaagtgac cccttaccta   240

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ccacaacttc tcttagtcca gacaatactt ccacccaagt atccccggac tctttggata   360

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ccaatgcaaa actcaaccct accccaggca gcaatgctat ctcagatgcc taccttaatg   540

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tatataacaa ggaaactaaa ttatttacag caaagctaaa tgttaatgag aatgtggaat   720

gtggaaacaa tacttgcaca aacaatgagg tgcataacct tacagaatgt aaaaatgcgt   780

ctgtttccat atctcataat tcatgtactg ctcctgataa gacattaata ttagatgtgc   840

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acagatttca gtgtggtaat atgatatttg ataataaaga aattaaatta gaaaaccttg   1020

aacccgaaca tgagtataag tgtgactcag aaatactcta ataataccac aagtttacta   1080

acgcaagtaa aattattaaa acagattttg ggagtccagg agagcctcag attatttttt   1140

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1224

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ttgcatccgg agagtggaca agaaaatgat gccaccagtc cccatttctc aacacgtcat    180

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1225

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taagatttgt aatatttctc tcttttttaga gaaatttgcc aatttacttt gttatttttc     1260

cccaaaaaga atgggatgat cgtgtattta ttttttttact tcctcagctg tagacaggtc     1320

cttttcgatg gtacatattt ctttgccttt ataatctttt atacagtgtc ttacagagaa     1380

aagacataag caaagactat gaggaatatt tgcaagacat agaatagtgt tggaaaatgt     1440

gcaatatgtg atgtggcaaa tctctattag gaaatattct gtaatcttca gacctagaat     1500

aatactagtc ttataatagg tttgtgactt tcctaaatca attctattac gtgcaatact     1560

tcaatacttc atttaaaata tttttatgtg caataaatg tatttgtttg tatttgtgt     1620

tcagtacaat tataagctgt ttttatatat gtgaaataaa agtagaataa acacaaaaaa     1680

aaaaaaaaaa aaaaaaaaaa aa                                              1702
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<210>   2867
<211>   563
<212>   DNA
<213>   Homo sapiens

<400>   2867
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gctcaggtgc cctacccttc accccttct gtatcagatt ggacctccca ctcccatctc      120
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1226

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actctgcgtg tacaatcttc catatccgca agttcactgg cactcttctg gcacctgggc    180

aagatcccag aacagaggat ggagtgactg gcctcacaga gcttagtgcc cgactcaggg    240

gaaatgggac tggtgcatgg gaaatggtca gcctaggata ggacacgaga gtctgaaatt    300

caaagcaacc agcttgaagt ggtttgagaa gctggaagca aacatgggct agagagatag    360

ggcagaagtc aagacgagga tctggactga tgtggagaca agtagccacg gaagcatgaa    420

ctgtatcctg cacaaagtcc ctcttccccg cctcctaatt cattatgccc aaaagtgctt    480

acgtgaaatt ccagcccaga gtactcatga cttgagagac gtggacggag ccagcttcta    540

ccttgcttgg acgtctctcc cct                                            563


<210>  2868
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<212>  DNA
<213>  Homo sapiens

<400>  2868
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ataacaaaac gtcatatgag aagcatggta gatccttagc atcaaaggtt gaggactctt    120

attctgatta taagtagtgg ctcttgacta caatcaagtc tcaaataata gtgtaagaga    180

ataaagcaga ataataagac taagttaaca gtttaggctt ctttggaatc atgcgggcct    240

agatgaaaat cccaacactg tcctttacta gctaagtgac cttgagcaac tgattacacc    300

ctttgatgcc tcagttttct cctctgtgtt gtggggtaat agtaatatct acttcctggg    360

gttgttcgtg aagattaatt aacaattata cttgtcaaag ctttagcaca gtgccctgta    420

tgttatttcc ttggccaaac tttcttactc tgccatttgt tcaatgtcct aatgagcatg    480

aacactacat taggtatcat gcagaacact ctaaagataa gtattatgat ctctatttca    540

cagataagga aatttaaact gggagaggct aaagggctga cttgcccaag gtcacttgaa    600

actaatatgc cagcagagac agaattagga gccaagtata tttaagagcc aagtgtattg    660

aacctaaaat ctgggctcct aaataccaag cttcactggc tctctggtcc cagtgagagt    720

tggtgctaaa aagtattccg gaatgaaaag ttctcttcca gagaccctgg ccttccaaag    780

cggtcacctg atagggaagt cttacggcta ggaagttaca aa                       822


<210>  2869
<211>  1182
<212>  DNA
<213>  Homo sapiens

<400>  2869
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ctggctcttg ccctcatcct ggttctggaa tcctcagttc aaggttatcc tacgcagaga    120

gccaggtacc aatgggtgcg ctgcaatcca gacagtaatt ctgcaaactg ccttgaagaa    180

aaaggaccaa tgttcgaact acttccaggt gaatccaaca agatcccccg tctgaggact    240

gacctttttc caaagacgag aatccaggac ttgaatcgta tcttcccact ttctgaggac    300

tactctggat caggcttcgg ctccggctcc ggctctggat caggatctgg gagtggcttc    360

ctaacggaaa tggaacagga ttaccaacta gtagacgaaa gtgatgcttt ccatgacaac    420

cttaggtctc ttgacaggaa tctgccctca gacagccagg acttgggtca acatggatta    480

gaagaggatt ttatgttata aaagaggatt ttcccacctt gacaccaggc aatgtagtta    540

gcatatttta tgtaccatgg ttatatgatt aatcttggga caaagaattt tatagaaatt    600

tttaaacatc tgaaaaagaa gcttaagttt tatcatcctt ttttttctca tgaattctta    660

aaggattatg ctttaatgct gttatctatc ttattgttct tgaaaatacc tgcatttttt    720

ggtatcatgt tcaaccaaca tcattatgaa attaattaga ttcccatggc cataaaatgg    780

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tcatacctaa attaagactc tgacttggat tgtgaattat aatgatatgc cccttttctt    900

ataaaaacaa aaaaaaaata atgaaacaca gtgaatttgt agagtggggg tatttgacat    960

attttacagg gtggagtgta ctatatacta ttacctttga atgtgtttgc agagctagtg   1020

gatgtgtttg tctacaagta tgattgctgt tacataacac cccaaattaa ctcccaaatt   1080

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gtattttcaa atgttactat atattaaagc agaaatataa cc                      1182
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<210>   2870
<211>   537
<212>   DNA
<213>   Homo sapiens

<400>   2870
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acaaaagcag cctttcacga ttatgtgagg gaacaaaggg caacaccctt attagtgcca    180

gtttaaaacc ttccttcaca ccctggactc tgccctatgt gcgtcctggt tgattttaac    240

ctacatccta acatttaggc cagtttcctt tcatccttct tacaaatata aaatctctta    300

cccttctcta atattatttg gcattccaaa ataaggaagt gtcatggtta aaaccaaatc    360

aaaggcaatt ctgactgtgc acagctcagc ctccacccaa cctcagaacc actggatcag    420

accaggtttt agtttttttg tacatttact tgataactaa gacacaattt gcctacagtg    480
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aaatgcttag ttctgacacg tatcgctcaa tccactgtca agaattcata acaaagt   537


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<211>  503
<212>  DNA
<213>  Homo sapiens

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tgaaagtcaa atcaaactga tctggcaacc ctatctagtt acctacaatc taccgtgttc        120

ccataaaggc tttaagtaat ttggaatccg ttaacacatt tagcttattc tttccccatt        180

ggttccctgg gcttagagca gacagcaagc ctttctttca cttggccaag aaggcacctc        240

cttttcccat ctaacaggtt gggatcacag ctagttggtg gcaaagcagt ccacatgcat        300

gttgtttatc ttttaagga tatggtcata gtttccaccc ctccttacct ctcctgactc        360

accatctcta agccttccca cacaggccct gctgcagccg ccggagaact gaccgtgctt        420

gtgggtccac tccctcctcc cacatcttcc ttaagcctca atccatccca gttcatccat        480

gccctttcca aagtcctgtg att                                              503


<210>  2872
<211>  448
<212>  DNA
<213>  Homo sapiens

<400>  2872
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aaagcaattt aataggcaca atcctacagg ttttctgaga gaaataagga agagatcaag        120

tgtaagctac gtaaaattca cgttttgcac cttataaagc aaacttcaat gttgttaaat        180

aaccagtaga aaatatctac aaaaatcaaa ctaaacacct gttcttataa gcagcagtcc        240

tctattttct ctctaaacca tatattccca actcagaccc tctctgtgac ccactgttcc        300

caaagcatag agtctgaaga agaaatataa aacatttcgg acattcgttc acaaaaccaa        360

attagacctt tccacaaagt acaggagata aaacagaaac acttccattt tatctaattt        420

atggcaaata gttcaaggaa tgcctatt                                          448


<210>  2873
<211>  449
<212>  DNA
<213>  Homo sapiens

<400>  2873
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atataaaaaa aaaaggatac tcacctgacc ctttcagatg tttaacgatt cgtcttcctc        120
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ctcggggatg cttttctga aggatgctgg cctggggaaa acagaaccgg aagggtaaca      180

cctgccatac ctaataaaac caatgagaaa tacgaggccc cgagatggag tttctgggag      240

attcctgaag agcacgctgt ggcgattgag atgatgacgc gtggagctgc cccctccct       300

gtctcccaca tcagggacct gtccctctac aggaggaatt ctactcctga ggccaccgtc      360

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gctgtttctg ccttcttgct ggtgaattt                                        449
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<211>    3362
<212>    DNA
<213>    Homo sapiens

<400>    2874
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tgtggagatc aggtcttctc caagaaaaaa aaaagaaaa aaaaaacaa catggctgca        120

aaggagaaac tggaggcagt gttaaatgtg gccctgaggg tgccaagcat catgctgttg      180

gatgtcctgt acagatggga tgtcagctcc tttttccagc agatccaaag aagtagcctt      240

agtaataacc ctcttttcca gtataagtat ttggctctta atatgcatta tgtaggttat      300

atcttaagtg tggtgctgct aacattgccc aggcagcatc tggttcagct ttatctatat      360

tttttgactg ctctgctcct ctatgctgga catcaaattt ccagggacta tgttcggagt      420

gaactggagt ttgcctatga gggaccaatg tatttagaac ctctctctat gaatcggttt      480

accacagcct aataggtca gttggtggtg tgtactttat gctcctgtgt catgaaaaca       540

aagcagattt ggctgttttc agctcacatg cttcctctgc tagcacgact ctgccttgtt      600

cctttggaga caattgttat catcaataaa tttgctatga tttttactgg attggaagtt      660

ctctattttc ttgggtctaa tcttttggta ccttataacc ttgctaaatc tgcatacaga      720

gaattggttc aggtagtgga ggtatatggc cttctcgcct tgggaatgtc cctgtggaat      780

caactggtag tccctgttct tttcatggtt ttctggctcg tcttatttgc tcttcagatt      840

tactcctatt tcagtactcg agatcagcct gcatcacgtg agaggcttct tttccttttt      900

ctgacaagta ttgcggaatg ctgcagcact ccttactctc ttttgggttt ggtcttcacg      960

gtttcttttg ttgccttggg tgttctcaca ctctgcaagt tttacttgca gggttatcga     1020

gctttcatga atgatcctgc catgaatcgg ggcatgacag aaggagtaac gctgttaatc     1080

ctggcagtgc agactgggct gatagaactg caggttgttc atcgggcatt cttgctcagt     1140

attatccttt tcattgtcgt agcttctatc ctacagtcta tgttagaaat tgcagatcct     1200

attgttttgg cactgggagc atctagagac aagagcttgt ggaaacactt ccgtgctgta     1260
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agcctttgtt tattttttatt ggtattccct gcttatatgg cttatatgat ttgccagttt    1320

ttccacatgg attttttggct tcttatcatt atttccagca gcattcttac ctctcttcag    1380

gttctgggaa cacttttttat ttatgtctta tttatggttg aggaattcag aaaagagcca    1440

gtggaaaaca tggatgatgt catctactat gtgaatggca cttaccgcct gctggagttt    1500

cttgtggccc tctgtgtggt ggcctatggc gtctcagaga ccatctttgg agaatggaca    1560

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ctggggtgga agagctttct tctccgcagg gatgctgtga ataagattaa atcgttaccc    1680

attgctacga aagagcagct tgagaaacac aatgatattt gtgccatctg ttatcaggac    1740

atgaaatctg ctgtgatcac gccttgcagt catttttttcc atgcaggctg tcttaagaaa    1800

tggctgtatg tccaggagac ctgccctctg tgccactgcc atctgaaaaa ctcctcccag    1860

cttccaggat taggaactga gccagttcta cagcctcatg ctggagctga gcaaaacgtc    1920

atgtttcagg aaggtactga acccccaggc caggagcata ctccagggac caggatacag    1980

gaaggttcca gggacaataa tgagtacatt gccagacgac cagataacca ggaaggggct    2040

tttgacccca aagaatatcc tcacagtgcg aaagatgaag cacatcctgt tgaatcagcc    2100

tagaggagaa gcagcaggaa tgatgctttg atactctgga ggagaagtta actcaagatg    2160

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ttatagaggt ttgtgaagaa aattcaacct cagcaacttc agaaactgcc cctgatacgt    2400

gtgagagaga aataaaatca gattttgagt gttgaaggga ctgaggaagt gaggataaag    2460

agcatgagga cagcatggaa agaaggaggc agaagtggaa ctgaactttc actctccatg    2520

ggacagatca atctcattat caagtctgaa tagcaaccag ccctctcctc cacccgtttt    2580

ctcctcagtt aattggagct cagtcaggtg attattgagt cttgtacagc actgaaatga    2640

aatcaaagat gaagaagcat tgattgtatt cgaagattga agcacgctca tactttgtat    2700

gtgctttagg gaaggggtgg gtgggcactt gggccttgcg ggtgcattca tgtaatctga    2760

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gtgtactttt caatcctgtg taatgtttaa ttcttgcaac tgaatcaaaa cagtgttaaa    3000

ttatggcaat atttgcactt tgggaatgag tacataactg tatgatcaca ctctgcaaat    3060

gccacttttta aagctgttaa tagactttgc acctttttctt tgacaaggat gtgtcatatt    3120
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taaatttta  cattcatcat  ggctacaggt  agaactgggg  aggggggaat  gtaatttttt     3180

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aagtgttttt  cagacctcgg  tattcctaat  gtgggatgtg  actttatttt  atttttagta     3300

gcaaatttgg  atgtagactg  acagacatag  ctgaatgtct  taataaattt  aaatttgaag     3360

at                                                                        3362
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<211>   591
<212>   DNA
<213>   Homo sapiens

<400>   2875
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cctggagtag  attgggagat  ttaggggata  tctgtccaaa  gatgagacag  tctgtttcta      180

gtttcccatc  cagcctgatg  gggcgtctac  agttgttacc  acaaggtgtc  gctgttgaac      240

agattctggt  gcagtctagt  gcatagctgt  ccacttctag  agtgatcact  tgctgggcca      300

agttcctctc  cttaagtggt  gtctcacatt  aaggttccca  aattacagac  tcattaattc      360

accctaataa  gctcatccag  gcagtttagg  tcttcagggg  cttccagcct  ccaacacaca      420

ttgggccaaa  accagcctgt  accaccagct  ccaagccctg  tgttgaatct  aggtcattgg      480

tccagatgcc  ccttcattct  gggcctgtgg  tgtcctttcc  agacagcaga  cctcagttaa      540

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<213>   Homo sapiens

<400>   2876
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atggatccaa  atttctggct  gcaagtgcag  gagtcagtga  cggtacagga  gggtttgtgc      120

gtcctcgtgc  cctgcacttt  cttccatccc  ataccctact  acgacaagaa  ctccccagtt      180

catggttact  ggttccggga  aggagccatt  atatccgggg  actctccagt  ggccacaaac      240

aagctagatc  aagaagtaca  ggaggagact  cagggcagat  tccgcctcct  tggggatccc      300

agtaggaaca  actgctccct  gagcatcgta  gacgccagga  ggagggataa  tggttcatac      360

ttctttcgga  tggagagagg  aagtaccaaa  tacagttaca  aatctcccca  gctctctgtg      420

catgtgacag  acttgaccca  caggcccaaa  atcctcatcc  ctggcactct  agaacccggc      480
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cactccaaaa accttacctg ctctgtgtcc tgggcctgtg agcagggaac accccgatc    540

ttctcctggt tgtcagctgc ccccacctcc ctgggcccca ggactactca ctcctcggtg    600

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aatgacaccc accctaccac agggtcagcc tccccgaaac accagaagaa ctccaagtta    960

catggcccca ctgaaacctc aagctgttca ggtgccgccc ctactgtgga gatggatgag   1020

gagctgcatt atgcttccct caactttcat gggatgaatc cttccaagga cacctccacc   1080

gaatactcag aggtcaggac ccagtgagga accctcaaga gcatcaggct cagctagaag   1140

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acacaagctc cttaaccttc catgtctcca ttttcttctc tgtgaagtag gtataagaag   1380

tcctatctca tagggatgct gtgagcatta aataaaggta cacatggaaa acaccag      1437
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<210> 2877
<211> 1182
<212> DNA
<213> Homo sapiens

<400> 2877
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tggtgctgag ctccccactg gctttggctg gggacacccg accacgtttc ttgtggcagc    180

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ggcgggccgc ggtggacacc tactgcagac acaactacgg ggttggtgag agcttcacag    420

tgcagcggcg agttgagcct aaggtgactg tgtatccttc aaagacccag cccctgcagc    480

accacaacct cctggtctgc tctgtgagtg gtttctatcc aggcagcatt gaagtcaggt    540

ggttccggaa cggccaggaa gagaaggctg gggtggtgtc cacaggcctg atccagaatg    600

gagattggac cttccagacc ctggtgatgc tggaaacagt tcctcggagt ggagaggttt    660
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acacctgcca agtggagcac ccaagtgtga cgagccctct cacagtggaa tggagagcac    720

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tcttccttgg ggccgggctg ttcatctact tcaggaatca gaaaggacac tctggacttc    840

agccaacagg attcctgagc tgaaatgcag atgaccacat tcaaggaaga accttctgtc    900

ccagctttgc agaatgaaaa gctttcctgc ttggcagtta ttcttccaca agagagggct    960

ttctcaggac ctggttgcta ctggttcggc aactgcagaa aatgtcctcc cttgtggctt   1020

cctcagctcc tgcccttggc ctgaagtccc agcattgatg acagcgcctc atcttcaact   1080

tttgtgctcc cctttgccta aaccgtatgg cctcccgtgc atctgtactc accctgtacg   1140

acaaacacat tacattatta aatgtttctc aaagatggag tt                      1182
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<210>  2878
<211>  2412
<212>  DNA
<213>  Homo sapiens

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gtaacccagg aggaagccca cggcgtcctg caccggcgcc ggcgcgccaa cgcgttcctg    180

gaggagctgc ggccgggctc cctggagagg gagtgcaagg aggagcagtg ctccttcgag    240

gaggcccggg agatcttcaa ggacgcggag aggacgaagc tgttctggat ttcttacagt    300

gatggggacc agtgtgcctc aagtccatgc cagaatgggg gctcctgcaa ggaccagctc    360

cagtcctata tctgcttctg cctccctgcc ttcgagggcc ggaactgtga gacgcacaag    420

gatgaccagc tgatctgtgt gaacgagaac ggcggctgtg agcagtactg cagtgaccac    480

acgggcacca gcgctcctg tcggtgccac gaggggtact ctctgctggc agacggggtg    540

tcctgcacac ccacagttga atatccatgt ggaaaaatac ctattctaga aaaaagaaat    600

gccagcaaac cccaaggccg aattgtgggg ggcaaggtgt gccccaaagg ggagtgtcca    660

tggcaggtcc tgttgttggt gaatggagct cagttgtgtg gggggaccct gatcaacacc    720

atctgggtgg tctccgcggc ccactgtttc gacaaaatca gaactggag gaacctgatc    780

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gcccccaaac tctcccccaa atgtatttct cccttcgctg ggtgccgggc tgcacagact   2340

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<213>  Homo sapiens

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acagctttac accaaagggc atcactatcc ctcaaagaga gaaacctgga cacatgtacc   240
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aaccaagtcc cgagaaaaga aagtgaatag tgttagcacg aggaggaagg aagaaatgga    180

gattagattg gatactcttt ctgcatcact gggtagatcc agcactttaa atgactgcaa    240

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tatttgcaaa acaccaatgg ggatgtggac aggaatgttg aacaataaag tgggaaactt   1020

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agatataaaa gagagtcacc tcattgaatt aaatattgaa aacccagatg acagaagaag   1260

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acctgagccc ctatccttga gctcagacat ctccttaaat aagtcacagt tagatgactg   1380

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ggaaatgttt tgtctttaag tgtaaatatt ttaaaatttg acataccccta atgttaataa   2160

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<210> 2881
<211> 1847
<212> DNA
<213> Homo sapiens

<400> 2881

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caacacctta gaaggtgttg cttaatttat ttctagaaaa gcagcccaga gtcagtcatt     360

gaagccttcc ccaccccctg gccaaaaaaa aaaaaaaaaa aaaactggac acattttgga     420

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<213>  Homo sapiens

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gctcctggaa gaccctcagc ctgcctgctg aggccatgtc ggactacgag aacgatgacg     180

agtgctggag cgtcctggag ggcttccggg tgacgctcac ctcggtcatc gacccctcac     240

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<212> DNA
<213> Homo sapiens

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ccctcacagg aaagaaagcc tgattcaaga aaacaaagtt tgaaacaagg catatttata       300

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<210>   2885
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<212>   DNA
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aaaaggtttt ttgattagtt cattattcat ttgaacatgg aaattatgct cactagtggc       360

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cttctacaag tcacctttta tttcaggcat ttgtaaatgc ccattaataa agtatggttc       480

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<210>   2886
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<212>   DNA
<213>   Homo sapiens
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<400> 2886

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ccctacaagg ggcacaaagg gatgacacca aacctggcag gaactttca cgcaatcaag      180

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aagcttctgc tgctcctcct cacctgcaaa gcttttctgc cacttttgcc tccttggaaa     480

actcttatcc atctctcaaa actccagcta ccacatcctt gcagccttcc ctcatatacc     540

cccactacta ctgtagccct gtccttccct ccagccccac tctggccctg gggctgggga     600

agtgtctgtg tccagctgtc tcccctgacc tcagggttcc ttggggggctg ggctgaggcc     660

tcagtacaga gggggctctg gaagtgtttg ttgactgaat aaacggaatt cagtgcgaaa     720

acaaaaaaat aggaaataaa agatctcgga aaatagcatt ttgttaaaac cttggggggt     780

aaaaccccgg ggagttttaa cggaaaaatt ccagggaaca caacttgggg gccaaa        836
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<210> 2887
<211> 742
<212> DNA
<213> Homo sapiens

<400> 2887

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aaatgatgga tataagtggt agctgtatct agtgaagtgt ctgtcagtaa gtgaaacatt     120

ttttggtggt ggcttatcca caaacagttt agttgtagaa taaaacttat gagtgacatc     180

tggaaagtaa ccatgctaag atggcaagca cactggaaac aattaggcca cttggctttc     240

ttttgctgta ttgttttata agcctacttt acctcccagt cttggaaaca agttttagtt     300

ttttattggt ttggagacta gagccaatag tataatgttc tcaaaggaaa cagacttgag     360

ttgttggatt agaggaacta acccaactta tatgattttg tttttggttt ttgtcgtgta     420

gttatggcac tgtcttattt ggaacatttg caactaggga taatacaaca tttttaactc     480

tcatttgaca acctactact aatcacagac cacaagggta atgaccaaat ttatgtggtt     540

tttgcactcc atagttgtct tagcccaatc tttctatact cttacgatta ctggggttaa     600

cgcttctgtg aggaccttct ggctcttgag ataccctaaa tatttacaga tacttagata     660

tcttgaagat agaataggat atcgagattg taccaaatag gaatatcagg agtatggtac     720
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1243

aaatgagcag atacctgttg aa   742

<210> 2888
<211> 440
<212> DNA
<213> Homo sapiens

<400> 2888
ttttttgggt tttaaggagt ttattgctaa tctgtaaaac agaaagagac aggagataag   60

catgacaaaa tatagggaag aaatgacttt tgcctaaact tccaaattgt gtacaattga   120

agcctctgct ttatagctct tagcacacct ctcaaataag aaggcagtac tgggaaggct   180

ctgaacctgt ggcagaacca ctgatagctg tggagctatt ccaaggagtc tgggaatcag   240

ggggattatc aagatcattg ttagaataaa ttaatcttac tgtatatata gcagaagttt   300

tcaagcatat gtaaatgcta ctaataacca ataattaca ccttgttttt ctttaaactg   360

taactctcaa gtatgtctct acataatttt ttgatggtag tgtctgcatg ctcaaaaagc   420

ttgaaaacac tactggagaa   440

<210> 2889
<211> 524
<212> DNA
<213> Homo sapiens

<400> 2889
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atacagcatc agtgcttcct ataatgtcca ggttaggaga gaagcaaatg gagctttact   120

aaggaagaga aagtgatcaa taccagtgag aaaggtgaaa aaaaaaaaa acaaacaaaa   180

acgaaaaaaa aacctaagca aattcagtga gaaagaaaa agcagaactt agagtcctta   240

cccttcaatt taaggaagga gagttattgc ctagcagaat cttgaaataa aatttcctta   300

gaaagcccca gaaagttttg tgtgtattgc aagtccaaag gataaggaga acttctatat   360

gctttcttct tatttccact gggcaaagta ctgctccatc aagactcagc ccgccatgag   420

gctttccaat caactctcaa ccaccacaac agttagggct ttttcctcta tgttgcaaag   480

cactttctgc ataactcaga atgcaaaatg tactcattca tttg   524

<210> 2890
<211> 575
<212> DNA
<213> Homo sapiens

<400> 2890
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt   60

tttttttggac ccaaaaaaaa aaaacttta aggaaggggg acccagttaa aaccccttcc   120

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aaatgcggcc caaccctgcc ccacggaaac cggccatggc aacccctaaa taaaaagggg    180

ttttttgaggc ggccggcccc cacccaaagg atgcccccaa ttttttttttg ccagggggga   240

atgtccttgg acacggggcc ccaaaattcc ccatgccggg ggtttgtact ttaaaagggc    300

ttcctaacct cctccgggtg ttcctaaggg ccatgctgga gctaaaactt gtaaaaaaag    360

gcccaggctt cccccaggtc cgagtaaatt ttcacagggg gggggaacca ccccctggcc    420

ttggggattt tccgttgact ccaaaacagt ttggccacgg ccagaaccac atggggggtaa   480

tgctcacact ttttaaggga atccacgctt tggggcctcc tgtgggggcct tgcctggagg   540

aagatggcct cacaccaaag gataccggag ttggg                              575
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<210>  2891
<211>  467
<212>  DNA
<213>  Homo sapiens


<220>
<221>  misc_feature
<222>  (428)..(428)
<223>  n is a, c, g, t or u

<400>  2891
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cctggccatt tttgcccgga tccccaagac cccggcgttg gcacggccca taccgaaact    120

atgcaagggt tcgaaattat cctttccctc acggacaact cgagctttct ccttattata    180

ctaccttccc taccggcatg accggaccgg tcacctgggg ggccacgcac atttctacag    240

gaaaactggc tcccttcttg ggggccgagg gcttcctgtg aaaaggatg agtttggagc      300

ggtactccct cagccggtgc acgttgatct ggagggactc cgcggacttg ctcctgctcc    360

tgggatccac aaaaatgcgc taaggtccgg cccaccttct tgggaatgcc gcccaccctg    420

agctcctnca ggatgaatcc gcggccgact cgcaccttct tgggtac                 467
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<210>  2892
<211>  473
<212>  DNA
<213>  Homo sapiens

<400>  2892
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acaggtctgc agctataaaa atcatctcga aaacatgaga tttcagagat ccagttctca    120

gtgttacctt gaagatgaca atttatgaag aaacaggtga ttttaatccg aaattgccag    180

gaaacaaatt actcctcaaa agcccttgga aagtaataag atagctaggc agaaaaaaaa    240

agattctgca aaactaaact taatgtgtat tcatctagac ctgaattaaa aataaaattc    300
```

```
cactataaaa agaatttttc aaaatgttag gcccaagaat atggccatat tgttccatct     360

tgaagaaccc agttgattca gtttcattac tggcctcccc actcttctaa gtaagtccct     420

cactataaac atttacgaat tccatctcag cattagtact aaacaatatt cat            473
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<210>  2893
<211>  546
<212>  DNA
<213>  Homo sapiens


<220>
<221>  misc_feature
<222>  (280)..(280)
<223>  n is a, c, g, t or u

<220>
<221>  misc_feature
<222>  (537)..(537)
<223>  n is a, c, g, t or u

<400>  2893
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ttgcttaatg ggagaacttg caaatgagat ttaaaacatt gtaattttta taaggtaaca     120

gaagctagat ccctttcact gttcatctca agctattgat cttgtcagtg ttgtacagat     180

ctagaatggg ttgtcaggga taaggtcact gatctgatgg tgattgttga catctgctga     240

ctccacacaa caaccctagg ggaccggtgc tttgagcatn cttattttca gatggtttgc     300

ccacttcatg cagttaacag ctgttggtgt tgggcttcaa atccaggtct ttcggacatc     360

aaatcccagc ctcttaacaa ctcaccaagc agtgattact actccccaac ataggggcag     420

tatgtacaag tcatgttgaa ctaatacagt ttctttcttt gataggaata ctaattttgt     480

tgaacaagaa aatatgtact ggataagagt aaggcatttg acaaggcgtc ctgtganatc     540

tgtgaa                                                               546
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<210>  2894
<211>  1993
<212>  DNA
<213>  Homo sapiens

<400>  2894
actcatttat accaggaaac agacaagaga acaagaggct gccgaagaca aaacttctct      60

gcaagcacct gtgcacagca atgtgcgtgg gcatctgtga gaagaagaga atctgtgaag     120

tttgagcaag cggccttccc aagatgtacc gaatatctca actgatgtca acaccagtag     180

caagttcttc caggttggaa agagaatatg ctggagagct gtctcccacg tgcattttcc     240

caagtttcac ctgtgattcc ctggatggtt accattcttt tgaatgcggc tccatagatc     300
```

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ccctgacagg ctcccactat acctgtcgcc gaagtcccag actcctcacc aatggctact    360

atatttggac tgaagacagc ttcctgtgcg acaaagatgg caacataact ctgaacccat    420

cccagaccag cgttatgtat aaggagaact tagttagtac ctccaaatct tggctgcatg    480

gaagtatctt tggtgacatc aactcttctc caagtgaaga caactggttg aaggggacca    540

ggaggttgga cacagaccat tgcaatggaa atgcagatga tttagactgt tcttctctga    600

ctgatgactg ggagtcaggg aagatgaatg cagagtctgt gatcacctcc tcttccagcc    660

acatcatatc tcagcctcct ggaggaaact cccatagctt gtctcttcag tcccagttga    720

cagcttctga acgtttccaa gagaatagtt cggatcattc agaaaccagg ttgttgcaag    780

aggtcttctt tcaggcaatc ctgcttgctg tgtgcttaat cacttctgca tgtgcaagat    840

ggtttatggg agaaatatta gccagtgtct tcacatgctc attgatgata actgtagctt    900

atgtgaaatc attgtttctc agccttgcca gctatttcaa aaccactgcc tgtgctcggt    960

ttgtcaaaat ttgacaacca tttaggaatg ccttcgatga atgtcctcca tctgaatatc   1020

tggaaattgt ccaacttgca gtctacttgg aatcaagtgt tttattggaa gggagtaagc   1080

gagtaatgga gaaaaagcca ttttagtttg actatgtgat tttaaaatga tctcagtttt   1140

tccatcaaaa ttataatatg ctcatgaaaa taatattaat ttgccttccc tttgcaaaca   1200

ccggcagttg aaaggaaaag gacggggaat gtgatggaaa agagaccgcc tggaataaat   1260

gtccccctat gattctttaa ggcagtggtt ctcgagcttg aattttcatt aggaaattct   1320

gtgaggagct tgtaaccaga tttctgggtc tgccacatgc acctatctct tgctgaattg   1380

ctttaataga ataatgagag caagtttgtc taactaatac caacctgaca acttgaataa   1440

caataaatgc aatttgtaca taaaatataa tgctgcaaaa gtttgtcatt cacctcagtg   1500

gagtgacttg atattaggtg gtaaccgtag atgatggtta atatgaaaat ggacaggaaa   1560

gaagcatttt ctgaaagtta tattcttttg aaccacgttc taaaccaagt ttttaatctt   1620

cttggggctc gtaattacct ttcactttaa tgtcacttaa agatataaca cagaaaaatg   1680

ccttgagggc aaaatatagg caaaacacca atgcgctttc aaatgcatga aaatggtgca   1740

gttgtaccct tgagccttga ctcaagggct gtagatgttc cctttccacc ccccacactt   1800

ggtgcgtgtt cacaaagcaa atatggcctg taattcaaat ttgttctatg tgatactctc   1860

tgagtaaaaa ctcatacatg cagaaaattg tctttgctcg aaatgataat gccaaaatat   1920

aactttatat ataatttgca tttagtacat ttttggttaa aaaataaact aataaataag   1980

tgaagtcatc agc                                                       1993
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<210> 2895

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<211>    521
<212>    DNA
<213>    Homo sapiens

<400>    2895
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aaagttgctc agatttatcc agacctcaca taagtttata gatttcaagt agccactgta         120

ttttattaca gaaaatacat tcttcaagag gaaaatgtta aggccatagc agctttcacc         180

ttagctatct aagcttgtat taggtcatca ttaaatagta tctgtatcat tcttatgtgt         240

tccgtaagtt atgccacaaa taccagacca agtacactca gtctagaaac aaaaaagtgg         300

gaaataaagg ttaaaacatt ctaataggtg taatgggctg atagatgact ttatattaca         360

aagctactta agacaattct acttttctag aatacaacgc attaatataa acatttgaaa         420

ttcagaagat ttggcctgtg gatgctttgt ttctcaatgc aattcttgtt aatatgttag         480

taagtaataa tttattaata ccaataataa aaaattaaca t                             521


<210>    2896
<211>·   1679
<212>    DNA
<213>    Homo sapiens

<400>    2896
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ctacaccgag gaaatgggct caggggacta tgactccatg aaggaaccct gtttccgtga         180

agaaaatgct aatttcaata aaatcttcct gcccaccatc tactccatca tcttcttaac         240

tggcattgtg ggcaatggat tggtcatcct ggtcatgggt taccagaaga aactgagaag         300

catgacggac aagtacaggc tgcacctgtc agtggccgac ctcctctttg tcatcacgct         360

tcccttctgg gcagttgatg ccgtggcaaa ctggtacttt gggaacttcc tatgcaaggc         420

agtccatgtc atctacacag tcaacctcta cagcagtgtc ctcatcctgg ccttcatcag         480

tctggaccgc tacctggcca tcgtccacgc caccaacagt cagaggccaa ggaagctgtt         540

ggctgaaaag gtggtctatg ttggcgtctg gatccctgcc ctcctgctga ctattcccga         600

cttcatcttt gccaacgtca gtgaggcaga tgacagatat atctgtgacc gcttctaccc         660

caatgacttg tgggtggttg tgttccagtt tcagcacatc atggttggcc ttatcctgcc         720

tggtattgtc atcctgtcct gctattgcat tatcatctcc aagctgtcac actccaaggg         780

ccaccagaag cgcaaggccc tcaagaccac agtcatcctc atcctggctt tcttcgcctg         840

ttggctgcct tactacattg ggatcagcat cgactccttc atcctcctgg aaatcatcaa         900

gcaagggtgt gagtttgaga acactgtgca caagtggatt tccatcaccg aggccctagc         960
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tttcttccac tgttgtctga accccatcct ctatgctttc cttggagcca aatttaaaac    1020

ctctgcccag cacgcactca cctctgtgag cagagggtcc agcctcaaga tcctctccaa    1080

aggaaagcga ggtggacatt catctgtttc cactgagtct gagtcttcaa gttttcactc    1140

cagctaacac agatgtaaaa gactttttt tatacgataa ataacttttt tttaagttac    1200

acatttttca gatataaaag actgaccaat attgtacagt ttttattgct tgttggattt    1260

ttgtcttgtg tttctttagt ttttgtgaag tttaattgac ttatttatat aaatttttt    1320

tgtttcatat tgatgtgtgt ctaggcagga cctgtggcca agttcttagt tgctgtatgt    1380

ctcgtggtag gactgtagaa aagggaactg aacattccag agcgtgtagt gaatcacgta    1440

aagctagaaa tgatccccag ctgtttatgc atagataatc tctccattcc cgtggaacgt    1500

ttttcctgtt cttaagacgt gattttgctg tagaagatgg cacttataac caaagcccaa    1560

agtggtatag aaatgctggt ttttcagttt tcaggagtgg gttgatttca gcacctacag    1620

tgtacagtct tgtattaagt tgttaataaa agtacatgtt aaacttactt agtgttatg    1679
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<210> 2897
<211> 450
<212> DNA
<213> Homo sapiens

<400> 2897
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ctgcaggaaa tgaagtgatt cagaactcac caattatgaa ctaaccttca atgccagagg     120

ctttaacagt ttctaataaa aattcagttc agatctcaag ttcagataag tctgaaaaaa     180

cacttcaagg tcatctgaac gaacatattc taccagtact ttatataatt gtatttacct     240

gttcctaaaa ctttccgtga aagaaatgtt gaattttctt cagaaatagt tttgagcaaa     300

atgtcaaaac aattctccca tgctcagtgt actttgact atactctgaa aatatttctt     360

cttgtttcc tgcacttacc tgttagtgtg ctcacactcc tgtattatgg aacatgttca     420

gtaactcata cacatgtaac acagaagtct                                     450
```

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<210> 2898
<211> 260
<212> DNA
<213> Homo sapiens

<400> 2898
ggcatgacta gaggtgtgac taataataat ccctcacatc tctatagcct aatacagttt      60

tccaagggtt ttctcatcca tgatctcatt tgatccttgc agcagtccta tgaggaaggc     120

agcacataca tcattagctc ccttttgcca aagaggaaac aaaaaacagg tgaaagggac     180
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ttgtctaagg gcacccagct ctaagggaca gagcaaagta acaggtcatt tctttttttc   240

atttattttt agagacagag   260

<210>   2899
<211>   452
<212>   DNA
<213>   Homo sapiens

<400>   2899
tttttttttt tttttttttt tttttttttt tttttttttt tttggaaatt ggaaagggca   60

aattaattaa gttttttaaa gccatcaagt tacaaagggc tattaggggt cttaaaaaga   120

caaagagtat ccaataaaac aaaaagcaat tccagatggt tttaggtgga acaattttgg   180

gccagttata tctataggcc attcctaatt tacttagcaa actttatccc ggggattggc   240

aaattaaaaa aaaggaagaa ccaacctata ttttcttttc ggttttttgg aaacagagcc   300

tccactctgt catccaggct ggagtacagg gggggatct cagctcaaca taccctcaac   360

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accaccgggc tcggccaatt ttttgcattt tt   452

<210>   2900
<211>   511
<212>   DNA
<213>   Homo sapiens

<220>
<221>   misc_feature
<222>   (500)..(500)
<223>   n is a, c, g, t or u

<400>   2900
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gatgttttaa cagagtggac aggtaataaa cacgttcaac aaaggcagat gttcttggag   120

gttaaatccc actaatcaac acgattaact ttaagggtcc tgagactttc aatagcatgt   180

acctcatgga ctaaaaaaga ggaagagttt atgcttcaca attaatctcc agaacttgac   240

acatgtaatt cttatcacca aggctttaga ttgaaaagta atagaaaaca acagtaactg   300

ttctggtaca gtctagcatt tccaatgtgc ttcttttat tttaatgaaa aaaaaagata   360

cattatatca aacaaaactg ttgatggatc cacatctttg caggctcttt gcggaatggc   420

tcaccaaata cacatttcca tctttagatc attatactgc ttaaacagca agatatgcta   480

aagagatatg aatatgattn tgacctacca t   511

<210>   2901
<211>   541

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<212>   DNA
<213>   Homo sapiens

<400>   2901
tttttttttt ttttttcct gacgtataca gatcatcctg gacagtttat ttctctaatt    60

ctgttaatca aagcagagat cagaacggat taactgtggc aacgtcgtat caggagcaca   120

aagagaagcc tgcctctttc agtttggtct tttctccagc aaaacagaaa tgcaatttag   180

tcaaacacat acagaggccc cactgtactg cctcactgat ggagggaaat acttgggtgc   240

aatcacacac agtgttagtg attggcaact gtccagtgct atttcgctaa aactggtaaa   300

aacagtttcc ttgggcaagc agctgattgg ctacttcata ctgtgctgag ttgggctcag   360

cttgtctgtc tctgggaggc cctaaggggc tcctcttttt cagctaggga taggggaga   420

ctgtcaacca gtatcttagc gtgaactgtc aatcgctgag cccctgccaa ggactctctg   480

gaagtccctc aggtatgctg aaaatacctt atactgaaaa ggtagctctc gctgcatcca   540

c                                                                   541


<210>   2902
<211>   646
<212>   DNA
<213>   Homo sapiens

<400>   2902
gaattaaaaa taatactttt attgctggtt atgctttctt aaaagtaaaa attattcttg    60

attgatgtga cttgccagaa tgtttgaaac accagtgacc aagggtcact atatctgccc   120

ccaaacaatt ccaccatgtt tacttatata gcactcacca aaccagaaga gaggctggga   180

tattctcagg ccactgcact gaacatcaat atgaaagaac catgaatgat gcgacaactg   240

agttgatttt ctacctcctc tgcccaccat gactttgcac cccaaattct ttcagtgtct   300

tttcaaggta caaccctcct tctgggcaca ggttggctgg tcacctcaa ggtatgttcc    360

ttcattctgc agtgatttcc tgcctctgct caattaagga agttgagaat acagataact   420

caggatcatg tttaattatg taaaaaagct ctaaagtcag gtaatggttt tcatgtgctt   480

ctcttgagca gtctgaggag agaatagaaa cagaaacccc ttggggcctg agtagacgca   540

gctggccatg cacaggcaga ggctcttggt cagtgcagga agcagagtca cagccatcgc   600

cttggggtgg ggatgaaatg agatgacctg ttggctgtat gacagc                  646


<210>   2903
<211>   557
<212>   DNA
<213>   Homo sapiens

<400>   2903
atctcaaagg caattgagtg ggtcttctgg gccagaccta tttaatttac gaaacatagt    60
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accttgcaga gaataggcat tgaaatatta tttaaacaat caaaccaaag atgttcttct    120

atcttcagct gtcagtgatc taatgccctc atctctctta tcctcaggac ccagaatggt    180

atattccaca taaaagatgc tttgtttatc aaatgaatca aaaagcacgc ctgaggcatt    240

tatttttact cctttacttc tgtaggccag gtcaaggtgg gtctaattca cttttatcat    300

cagcacttaa gaaactggat ggaagaccac aacaccttgt tttttgcaaa aattttccat    360

ctcctcaatc aggccaggaa gcatgtatct tctggacagg actttatctc tctactcagc    420

ttagtacact gccttatatt agtccatttg tcccatgttt tcatcactga ataaacttgt    480

taaatgactt ttggtctgga tctcacacct atattacttc atttccttct gtgagcactc    540

tataatgata acatcat                                                   557
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<211>  488
<212>  DNA
<213>  Homo sapiens


<220>
<221>  misc_feature
<222>  (239)..(239)
<223>  n is a, c, g, t or u

<400>  2904
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tgcgcgtggg tcgcgaggtg acaggagccg gccctcgtcc ttaatggagc ggccagagct    120

gggtggggc ggcccgggag ctcggggttc ccggcactac ctgaatgcag cccgaagcca    180

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ggtgtctcca acctcgagtt ggagaaccat gttgagtcag ttccccggaa ccttacaaat    300

ggactccact tcccccgttc ccattctacc gtttttttta aaaaatgatt tttttgagtg    360

gcggttccag gattagtcaa atagcttctc ccgagaatgc tctttaaaag attgtcagac    420

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<213>  Homo sapiens

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gtgactgtcc tgtctctcct catgctagta gctgccttct gctctccagc gctctcagca   180

ccaatgggct cagaccctcc caccgcctgc tgcttttctt acaccgcgag gaagcttcct   240

cgcaactttg tggtagatta ctatgagacc agcagcctct gctcccagcc agctgtggta   300

ttccaaacca aagaagcaa gcaagtctgt gctgatccca gtgaatcctg ggtccaggag   360

tacgtgtatg acctggaact gaactgagct gctcagagac aggaagtctt cagggaaggt   420

cacctgagcc cggatgcttc tccatgagac acatctcctc catactcagg actcctctcc   480

gcagttcctg tcccttctct taatttaatc tttttttatgt gccgtgttat tgtattaggt   540

gtcatttcca ttatttatat tagtttagcc aaaggataag tgtcctatgg ggatggtcca   600

ctgtcactgt ttctctgctg ttgcaaatac atggataaca catttgattc tgtgtgtttt   660

ccataataaa actttaaaat aaaatgcaga cagtta   696

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<211> 347
<212> DNA
<213> Homo sapiens

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tatttgtcat ctgaactact tttctatctt ttacctcctc caatagataa gttattagaa   180

ggcaaatatt gcttcttgat tttttgtttt ccgtctatct aagcttgaat tttatgtgca   240

cgtaaggtag atgtgaaatt catgggcatc aaatatgggt gggtaaaata taattttgtt   300

ttctataatt aaaattattc tatatctaga tccttgttgc attgggg   347

<210> 2907
<211> 549
<212> DNA
<213> Homo sapiens

<400> 2907
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aaatgtctgt gtgcatgtgc cctgagcaca cagggtggca taactcggca cactcataat   120

gacacagccg ttcacccagc cacagatagt gacagggcac acatggcgac acccacatgt   180

acggagataa atctccccca ccatgacatg ggtagacaga aaacacgccg cagtatactc   240

tagtatgttt acacaaacag ggagacaggc ccgtgcaatg catgtcacca acacccacac   300

tcagagtgac atctgctgga ggtgctcaga cacagccacc caccgtgaca tgccgagact   360

cacatatgtc acatgacaca ggcatgcatg ccacattcac tgtgactctc agtcctattc   420

attcatcacc tttctgggag atacactgaa atgtccaccc tttgcaaaat gcacacacac   480

gcgcacgcac acacgcacac acacgaacac acgcgcacac acgcacacac acgcacgcag   540

gtgtacaca   549

<210> 2908
<211> 400
<212> DNA
<213> Homo sapiens

<400> 2908
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gttcagagga cagaataatg aatcttcttt ctttccttct ttcttccttc cttccttctt   120

tccttccttc cttcccttt cctatggaca gctgagaatc attttctaac tttatcaaat   180

atgctccctc ctcttaagat agcctgccct ggctgcttcc tatgtctctt gcagtctgac   240

caggcactgt agggaagagg cccaaatgca cccacctggc ccagatatcc agaggccaag   300

gccacggtcc tgcaccacag cgtgagagtt cttctttgca gtgcctacaa acctatgctt   360

gcccccaaac tcgctcaggg gtaacggggt tggggaaaga   400

<210> 2909
<211> 547
<212> DNA
<213> Homo sapiens

<400> 2909
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caatgttgaa aacttagtat gaatgtgaac ctcactagat gttcaaatct ggtagagtgc   120

aaatttgtt catactattt tacatttta caaactcaaa tcactttggt tcatatattt   180

tctataaact attggcaaaa aaatcctcaa atttacattc ttttggctac attatttcta   240

acagatatag atttacttcc ggtttcggag agaaagactt attgtgtgtg cgtgatcaag   300

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tgacatcttc attggaaatt tttttcatgt aactgttttc attttcagaa aatatataag   420

ggggtcattc caaagttcag aatgatccta ttttttaaa aaacaaaatt cctgtaaaac   480

aaattaactc caggaactta aaatttactc caagacattt ccctcaaaac aaagcaaaaa   540

accccag   547

<210> 2910
<211> 549
<212> DNA
<213> Homo sapiens

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attcgctatt catcacaccc cgaagattga gatccactgt atttacacaa agcaaagcca    180

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gtgttccttt ttggaaacca acaacacatc tttaatacct acacacacac acatctctac    300

ctttaaaaaa aaaaaaaaag tgtaacttca cagatagtac ctaatcttca agcttaaaat    360

ttaagttaaa attaatctct attttgtggg cacccttttag tgaactaaaa tctacatgaa    420

accttttggc ttttgtgtag caggaaatac ccacgttttg ggtcaattag tgcagatggg    480

agcagcagag gagctacacc agacagcaaa gcaagactag agcaaacgag aaggaccagc    540

ccctagccc                                                          549


<210> 2911
<211> 408
<212> DNA
<213> Homo sapiens

<400> 2911
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ttcgcggcgt ggcgcccggt ggtccccaag gggagggaag ggggaggcgg ggcgaggaca    120

gtgaccggag tctcctcagc ggtggctttt ctgcttggca gcctcagcgg ctggcgccaa    180

aaccggactc cgcccacttc ctcgcccctg cggtgcgagg gtgtggaatc ctccagacgc    240

tgggggaggg ggagttggga gcttaaaaac tagtaccccct ttgggaccac tttcagcagc    300

gaactctcct gtacaccagg ggtcagttcc acagacgcgg gccaggggtg ggtcattgcg    360

gcgtgaacaa taatttgact agaagttgat tcgggtgttt ccggaagg               408


<210> 2912
<211> 525
<212> DNA
<213> Homo sapiens

<400> 2912
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ctatcttcag ctgtcagtga tctaatgccc tcatctctct tatcctcagg acccagaatg    180

gtatattcca cataaaagat gctttgttta tcaaatgaat caaaaagcac gcctgaggca    240

tttattttta ctcctttact tctgtaggcc aggtcaaggt gggtctaatt cacttttatc    300

atcagcactt aagaaactgg atggaagacc acaacacctt gttttttgca aaaattttcc    360

atctcctcaa tcaggccagg aagcatgtat cttctggaca ggactttatc tctctactca    420
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gcttagtaca ctgccttata ttagtccatt tgtcccatgt tttcatcact gaataaactt      480

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<210>  2913
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<212>  DNA
<213>  Homo sapiens

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tgaattggag attcaagcct attgttatct tatgaacact tcagcaaaca ggtctgccat      120

tcttaaaaat ataatgcttt gttggacaaa agggacaagc cacgtcccct ggtcctctcc      180

tctattcgcc tgtgaactcc atccacacgt aaaggacctc tgggtctgac tgtcccctcc      240

acaggcatgg tgctgggaaa aggaaacagg catatctggc ttttcagatt ttaaaccgga      300

aactctcaca gtcacaaatc caccatgaga cttgggagat tggatgagct gtctcccaaa      360

ccctaacacc ttccaccttc tcaaaatgaa ggctgccctt tcactgggag gttctgaatg      420

cgggattggt gctgactcag ctgggcaca aaggagaaca ggaggacatg gaaaatccga       480

caattcgaag tacaaatatt tcaaacacat gtgaaaacca tttggaaaga agaaaagagg      540

tatctggaat gatttcatga cagaaatgaa aaaagataaa tttagttcta atcttcctgg      600

caacaaagcc ccagaggaga aggtttcatt gtctgaagat aaaaacacac ccgtttgcct      660

ggatatgaac acagtattcc tgcaccaaat tctagaaaga atatactttc ttctaacaaa      720

gccaagagtt tttcttgtac tcattacagg gggcttttaa tcctaacata tttttaact      780

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cgtcaaatct attaactcct taacgaaccg aattaaggac caaaaacaaa ccttgttttt      900

tcacaaaggt tggatgttgt aaacgtccga aagtgtcctt ttatacgaaa gacagtaatc      960

tggggaaata tttactggaa tgacacaggt ctttggggga aggaactatt taccggataa     1020

atgggaaaag aaatgttagc gagactatgg tataacacgg ctaggagat aacaaataaa      1080

tatta                                                                  1085


<210>  2914
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<212>  DNA
<213>  Homo sapiens

<400>  2914
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ccgcctccca ggatcgtccg ccggtcaggg cccttgccct ccccggcaca ggccaccatg      120

gccaccaacc cacagccgca gccgcctcct ccggcgccgc gcctccccc gccgcagccg      180
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1256

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cagccgcagc caccgccgcc gccgccgggc cccggggctg gccccggcgc gggcggggcg    240

ggcggcgcgg gtgcgggcgc cggggacccg cagctcgtgg ccatgatcgt gaaccacctc    300

aagagccagg ggctcttcga ccagttccgc agagactgcc tggccgacgt ggacaccaag    360

cctgcgtatc agaatctgag acagcgtgtt gacaactttg ttgcaaatca cttggcaact    420

cacacatgga gtccgcatct caataagaac cagctaagaa acaacattag acaacaagtc    480

ctcaaatcag gaatgttgga gtctggtatt gaccgaatta tttctcaggt tgtggaccca    540

aagatcaacc acacattcag acctcaggta gagaaagctg tgcatgagtt tttggccacg    600

ctaaatcaca aagaggaagg aagtggcaac acagctcccg atgatgagaa accagacact    660

tcccttatta cacaaggtgt tcctactcct gggcccagtg ctaatgtagc caatgatgcc    720

atgtcgatat tggaaaccat aacttctctt aaccaagaag ccagtgctgc tagggcttca    780

acagaaacat caaatgccaa gaccagtgag agagcgtcaa aaaaacttcc atctcagcca    840

accactgata ctagtactga caaagaaaga acttcagagg acatggctga taaagaaaaa    900

tctacagctg actctggagg tgaaggactg gaaacagccc caaagtctga agagttcagc    960

gacctcccct gtccagtcga agaaattaaa aattacacaa aagagcataa taatttaatt   1020

ctgctaaata aggatgttca acaggaaagc agtgagcaaa aaataaatc aacagacaaa    1080

ggtgaaaaga agccagacag caatgagaaa ggagaaagaa agaaagaaaa gaaggaaaag    1140

actgaaaaga aatttgatca ctcaaaaaag agtgaagata cacagaaagt taaagatgaa   1200

aaacaagcaa aggaaaaaga agtagagagt ttaaaacttc cttcagaaaa gaacagtaat   1260

aaagctaaaa ctgttgaagg gacaaaagaa gatttctctt tgatagattc tgatgtggat   1320

ggacttacag acatcacagt tagctctgtt cataccagtg acctttcatc ttttgaagaa   1380

gatactgagg aggaagttgt aacgtctgat agcatggaag aaggagagat tacgtcagat   1440

gatgaagaga agaacaaaca gaataaaaca aaaactcaaa ctagtgattc tagtgaagga   1500

aaaacaaaaa gtgtacggca tgcgtatgtc cacaaaccat atctttactc aaaatactat   1560

agtgattctg atgatgagct tactgtagaa caacgacgac agtccattgg tattttgtgg   1620

ttttaggcca aagaaaaaga agagaggctt ttaagaaggc aaatcaatag agaaaaactt   1680

gaagaaaaac gaaaacagaa agcagaaaag acaaagtctt caaaaaccaa gggtcaaggc   1740

aggagtagtg tggacttaga agaatcatca acaaagagtt tggaacctaa agccgccaga   1800

attaaagaag tccttaaaga acggaaagtt ttagaaaaaa aagtagcctt aagcaaaaag   1860

agaaaaaaag attcaaggaa tgttgaagag aactccaaaa agaaacagca atatgaagaa   1920

gattccaaag aaacccttaa aacaagtgag cattgtgaaa aggaaaaaat ttcttcttca   1980
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1257

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aaggagctga agcatgttca tgcaaaaagt gaaccaagta aacctgcccg gagactttca    2040

gagtctttgc atgtagttga cgaaaacaaa aatgaatcca aattagaaag agaacataaa    2100

agacggacat ctacccctgt tatcatggag ggggtacagg aagagactga cacaagagat    2160

gtaaaaggc aagtagaacg ctcagaaatt tgcaccgaag agccccagaa acagaaaagc     2220

acacttaaaa acgaaaagca tctaaagaaa gatgattctg aaacaccaca tttgaaaagc    2280

ctacttaaga aagaggtgaa atcctccaag gagaagcctg aaagagagaa aactccatcg    2340

gaagacaaat tgtctgtgaa acataaatat aaaggtgatt gtatgcataa aacaggtgat    2400

gagactgagc ttcactcttc tgagaaaggt ttaaaagtag aggaaaatat tcaaaagcaa    2460

agtcaacaaa caaagctttc ttcagatgat aaaaccgaac gaaaaagtaa acataggaat    2520

gaaaggaaat tatcagtatt aggcaaagat ggaaagccag tttctgaata tattataaaa    2580

acagatgaga atgttcgtaa agaaaaaaaa                                      2610
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<212>    DNA
<213>    Homo sapiens


<220>
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<222>    (86)..(118)
<223>    n is a, c, g, t or u

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ctcattcaag ggtatgttta ctggtnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnac    120

tgtaaaagga tagtgtttgc atctagagga ctagagacat gcctgcacat ccctcacctt    180

caaaggtgaa ctctacacag gattcttgtc ctagtcattg tggcaacccc atctgacacc    240

ttgtgtagta cctcggccgc gaccacgcta atcactagt                           279
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<210>    2916
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<212>    DNA
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taacaggatc tcctcttgca gtctgcagcc caggacgctg attccagcag cgccttaccg    120

cgcagcccga agattcacta tggtgaaaat cgccttcaat acccctaccg ccgtgcaaaa    180

ggaggaggcg cggcaagacg tggaggccct cctgagccgc acggtcagaa ctcagatact    240

gaccggcaag gagctccgag ttgccaccca ggaaaaagag ggctcctctg ggagatgtat    300
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gcttactctc ttaggccttt cattcatctt ggcaggactt attgttggtg gagcctgcat        360

ttacaagtac ttcatgccca agagcaccat ttaccgtgga gagatgtgct tttttgattc        420

tgaggatcct gcaaattccc ttcgtggagg agagcctaac ttcctgcctg tgactgagga        480

ggctgacatt cgtgaggatg acaacattgc aatcattgat gtgcctgtcc ccagtttctc        540

tgatagtgac cctgcagcaa ttattcatga ctttgaaaag ggaatgactg cttacctgga        600

cttgttgctg gggaactgct atctgatgcc cctcaatact tctattgtta tgcctccaaa        660

aaatctggta gagctctttg gcaaactggc gagtggcaga tatctgcctc aaacttatgt        720

ggttcgagaa gacctagttg ctgtggagga aattcgtgat gttagtaacc ttggcatctt        780

tatttaccaa ctttgcaata acagaaagtc cttccgcctt cgtcgcagag acctcttgct        840

gggtttcaac aaacgtgcca ttgataaatg ctggaagatt agacacttcc ccaacgaatt        900

tattgttgag accaagatct gtcaagagta agaggcaaca gatagagtgt ccttggtaat        960

aagaagtcag agatttacaa tatgacttta acattaaggt ttatgggata ctcaagatat       1020

ttactcatgc atttactcta ttgcttatgc cgtaaaaaaa aaaaaaaaaa aaaaaaaaa        1080

aa                                                                     1082
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<210>  2917
<211>  610
<212>  DNA
<213>  Homo sapiens


<220>
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<223>  n is a, c, g, t or u

<220>
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<223>  n is a, c, g, t or u

<220>
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<400>  2917
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ttgaacaata cttgtctctc agtaaatagt aaagaccatc acaaaataaa aggtattctt        120

atttgttatt atttaataga agacacattc tctggtccat ttatatcctg tatacaaatt        180

aacttatttt gattgtatcc atgcaatcta agacaataaa aatagaagaa aaaacagcca        240

cataaacagc aaagtgttat tactgattta attgaattga tttgacattt tcagtccact        300
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1259

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gatatatttc ctgagataaa agttgcccct agtattcatg aatctgtagt tcattcttag      360

taatttaac atgaaaaatt gatgtgttta aattttcact ttaatattca tgttttctat      420

aaaatattgt aaaattctaa gatattatgg ttatacatat ttattactat tattacatat      480

taatgtgaat tttgagaaac tttcctttgc atgattttct caaattacaa aatatattat      540

tctcttataa aggacagcaa gtttaaaatg gagcaaggag cattggaaat atatttaaag      600

ggaangangg                                                            610
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<210>  2918
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<212>  DNA
<213>  Homo sapiens

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caccgcatct ggagaaccag cggttaccat ggaggggatc agtatataca cttcagataa      120

ctacaccgag gaaatgggct caggggacta tgactccatg aaggaaccct gtttccgtga      180

agaaaatgct aatttcaata aaatcttcct gcccaccatc tactccatca tcttcttaac      240

tggcattgtg ggcaatggat tggtcatcct ggtcatgggt taccagaaga aactgagaag      300

catgacggac aagtacaggc tgcacctgtc agtggccgac ctcctctttg tcatcacgct      360

tcccttctgg gcagttgatg ccgtggcaaa ctggtacttt gggaacttcc tatgcaaggc      420

agtccatgtc atctacacag tcaacctcta cagcagtgtc ctcatcctgg ccttcatcag      480

tctggaccgc tacctggcca tcgtccacgc caccaacagt cagaggccaa ggaagctgtt      540

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caatgacttg tgggtggttg tgttccagtt tcagcacatc atggttggcc ttatcctgcc      720

tggtattgtc atcctgtcct gctattgcat tatcatctcc aagctgtcac actccaaggg      780

ccaccagaag cgcaaggccc tcaagaccac agtcatcctc atcctggctt tcttcgcctg      840

ttggctgcct tactacattg ggatcagcat cgactccttc atcctcctgg aaatcatcaa      900

gcaagggtgt gagtttgaga acactgtgca caagtggatt tccatcaccg aggccctagc      960

tttcttccac tgttgtctga accccatcct ctatgctttc cttggagcca aatttaaaac     1020

ctctgcccag cacgcactca cctctgtgag cagagggtcc agcctcaaga tcctctccaa     1080

aggaaagcga ggtggacatt catctgtttc cactgagtct gagtcttcaa gttttcactc     1140

cagctaacac agatgtaaaa gactttttt tatacgataa ataactttt tttaagttac      1200

acattttca gatataaaag actgaccaat attgtacagt ttttattgct tgttggattt      1260
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ttgtcttgtg tttctttagt ttttgtgaag tttaattgac ttatttatat aaattttttt   1320

tgtttcatat tgatgtgtgt ctaggcagga cctgtggcca agttcttagt tgctgtatgt   1380

ctcgtggtag gactgtagaa aagggaactg aacattccag agcgtgtagt gaatcacgta   1440

aagctagaaa tgatccccag ctgtttatgc atagataatc tctccattcc cgtggaacgt   1500

ttttcctgtt cttaagacgt gattttgctg tagaagatgg cacttataac caaagcccaa   1560

agtggtatag aaatgctggt ttttcagttt tcaggagtgg gttgatttca gcacctacag   1620

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<210>   2919
<211>   2232
<212>   DNA
<213>   Homo sapiens

<400>   2919
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aatgtccgca tcgcaaccac cgccctggcc atctaccatg tgatcatgag cgtcttgttg    180

ttcatcgagc actcagtaga ggtggcccat ggcaaggcgt cctgcaagct ctcccagatg    240

ggctacctca ggatcgctga cctgatctcc agcttcctgc tcatcaccat gctcttcatc    300

atcagcctga gcctactgat cggcgtagtc aagaaccggg agaagtacct gctgcccttc    360

ctgtccctgc aaatcatgga ctatctcctg tgcctgctca ccctgctggg ctcctacatt    420

gagctgcccg cctacctcaa gttggcctcc cggagccgtg ctagctcctc caagttcccc    480

ctgatgacgc tgcagctgct ggacttctgc ctgagcatcc tgaccctctg cagctcctac    540

atggaagtgc ccacctatct caacttcaag tccatgaacc acatgaatta cctccccagc    600

caggaggata tgcctcataa ccagttcatc aagatgatga tcatcttttc catcgccttc    660

atcactgtcc ttatcttcaa ggtctacatg ttcaagtgcg tgtggcggtg ctacagattg    720

atcaagtgca tgaactcggt ggaggagaag agaaactcca agatgctcca agaggtggtc    780

ctgccgtcct acgaggaagc cctgtctttg ccatcgaaga ccccagaggg gggcccagca    840

ccacccccat actcagaggt gtgaccctcg ccaggcccca gccccagtgc tgggagggggt  900

ggagctgcct cataatctgc ttttttgctt tggtggcccc tgtggcctgg gtgggccctc   960

ccgcccctcc ctggcaggac aatctgcttg tgtctccctc gctggcctgc tcctcctgca   1020

gggcctgtga gctgctcaca actgggtcaa cgctttaggc tgagtcactc ctcgggtctc   1080

tccataattc agcccaacaa tgcttggttt atttcaatca gctctgacac ttgtttagac   1140

gattggccat ctaaagttg gtgagtttgt caagcaacta tcgacttgat cagttcagcc    1200
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1261

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aagcaactga caaatcaaaa acccacttgt cagttcagta aaataatttg gtcaaacaac   1260

agtctattgc attgatttat aaatagttgt cagttcacat agcaatttaa tcaagtaatc   1320

attaattagt taccccctat atataaatat atgtaatcaa tttcttcaaa tagcttgctt   1380

acatgataat caattagcca accatgagtc atttagaata gtgataaata gaatacacag   1440

aatagtgatg aaattcaatt taaaaaatca cgttagcctc caaaccattt aattcaaatg   1500

aacccatcaa ctggatgcca actctggcga atgtaggacc tctgagtggc tgtataattg   1560

ttaattcaaa tgaaattcat ttaaacagtt gacaaactgt cattcaacaa ttagctccag   1620

gaaataacag ttatttcatc ataaaacagt cccttcaaac acacaattgt tctgctgaag   1680

agttgtcatc aacaatccaa tgctcaccta ttcagttgct ctgtggtcag tgtggctgca   1740

tagcagtgga ttccatgaaa ggagtcattt tagtgatgag ctgccagtcc attcccaggc   1800

caggctgtcg ctggccatcc attcagtcga ttcagtcata ggcgaatctg ttctgcccga   1860

ggcttgtggt caagcaaaaa ttcagccctg aaatcaggca catctgttcg ttggactaaa   1920

cccacaggtt agttcagtca aagcaggcaa ccccccttgtg ggcactgacc ctgccactgg  1980

ggtcatggcg gttgtggcag ctggggaggt ttggccccaa cagccctcct gtgcctgctt   2040

ccctgtgtgt cggggtcctc cagggagctg acccagaggt ggaggccacg gaggcagggt   2100

ctctggggac tgtcgggggg tacagaggga gaaggctctg caagagctcc ctggcaatac   2160

ccccttgtgt aattgctttg tgtgcgacag ggaggaagtt tcaataaagc aacaacaagc   2220

ttcaaggaat tc                                                      2232
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<210>   2920
<211>   1620
<212>   DNA
<213>   Homo sapiens

<400>   2920
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ccttcagcgg ttcccaggct ccctacctga gtccagctgt ccccttttct gggactattc    120

aaggaggtct ccaggacgga cttcagatca ctgtcaatgg gaccgttctc agctccagtg    180

gaaccaggtt tgctgtgaac tttcagactg gcttcagtgg aaatgacatt gccttccact    240

tcaaccctcg gtttgaagat ggagggtacg tggtgtgcaa cacgaggcag aacggaagct    300

gggggcccga ggagaggagg acacacatgc ctttccagaa ggggatgccc tttgacctct    360

gcttcctggt gcagagctca gatttcaagg tgatggtgaa cgggatcctc ttcgtgcagt    420

acttccaccg cgtgcccttc accgtgtgg acaccatctt cgtcaatggc tctgtgcagc     480

tgtcctacat cagcttccag cctcccggcg tgtggcctgc caacccggct cccattaccc    540
```

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agacagtcat ccacacagtg cagagcgccc ctggacagat gttctctact cccgccatcc    600

cacctatgat gtaccccac cccgcctatc cgatgccttt catcaccacc attctgggag     660

ggctgtaccc atccaagtcc atcctcctgt caggcactgt cctgcccagt gctcagaggt    720

tccacatcaa cctgtgctct gggaaccaca tcgccttcca cctgaacctc cgttttgatg    780

agaatgctgt ggtccgcaac acccagatcg acaactcctg ggggtctgag gagcgaagtc    840

tgccccgaaa aatgcccttc gtccgtggcc agagcttctc agtgtggatc ttgtgtggag    900

ctcactgcct caaggtggcc gtggatggtc agcacctgtt tgaatactac catcgcctga    960

ggaacctgcc caccatcaaċ agactggaag tggggggcga catccagctg acccatgtgc   1020

agacataggc ggcttcctgg ccctggggcc ggggctgggg gtgtggggca gtctgggtcc   1080

tctcatcatc cccacttccc aggcccagcc tttccaaccc tgcctgggat ctgggcttta   1140

atgcagaggc catgtccttg tctggtcctg cttctggcta cagccaccct ggaacggaga   1200

aggcagctga cggggattgc cttcctcagc cgcagcagca cctggggctc cagctgctgg   1260

aatcctacca tcccaggagg caggcacagc cagggagagg ggaggagtgg gcagtgaaga   1320

tgaagcccca tgctcagtcc cctcccatcc cccacgcagc tccaccccag tcccaagcca   1380

ccagctgtct gctcctggtg ggaggtggcc tcctcagccc ctcctctctg accttttaacc   1440

tcactctcac cttgcaccgt gcaccaaccc ttcacccctc ctggaaagca ggcctgatgg   1500

cttcccactg gcctccacca cctgaccaga gtgttctctt cagaggactg gctcctttcc   1560

cagtgtcctt aaaataaaga aatgaaaatg cttgttggca aaaaaaaaa aaaaaaaaa    1620
```

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<210> 2921
<211> 916
<212> DNA
<213> Homo sapiens

<400> 2921
acttctcgct cgacacagcc agagctggag gtgggtgccc ggcacggagg ggcctgcgga     60

ccaatggctc tgccctgcac cttagggctc gggatgctgc tggccctgcc aggggccttg    120

ggctcgggtg gcagcgcgga ggacagcgtg ggctccagct ctgtcaccgt tgtcctgctg    180

ctgctgctgc tcctactgct ggccactggc ctagcactgg cctggcgccg cctcagccgt    240

gactcagggg gctactacca cccggcccgc ctaggtgccg cgctgtgggg ccgcacgcgg    300

cgcctgctct gggccagccc cccaggtcgc tggctgcagg cccgagctga gctggggtcc    360

acagacaatg accttgagcg acaggaggat gagcaggaca cagactatga ccacgtcgcg    420

gatggtggcc tgcaggctga ccctggggaa ggcgagcagc aatgtggaga ggcgtccagc    480

ccagagcagg tccccgtgcg ggctgaggaa gccagagaca gtgacacgga gggcgacctg    540
```

```
gtcctcggct cccaggacc agcgagcgca gggggcagtg ctgaggccct gctgagtgac    600

ctgcacgcct ttgctggcag cgcagcctgg gatgacagcg ccagggcagc tggggccag     660

ggcctccatg tcaccgcact gtagaggccg gtcttggtgt cccatccctg tcacagccgc    720

tcactccccg tgcctctgct tcccaagatg ccatggctgg actggacccc cagcccacat    780

gaccatgcct cagactgtca cccctaccag ttcccaagtc catgtgtacc ccgctcacca    840

cgggaacggc cccccccaac cacaggcatc aggcaaccat ttgaaataaa actccttcag    900

cctgtgaaaa aaaaaa                                                    916
```

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<210>    2922
<211>    1272
<212>    DNA
<213>    Homo sapiens

<400>    2922
gaattcggcc aaagaggcct atgcttctct gaagacttgc agcaaggctt gctgaggctc     60

acagaagata gccccagtgt tttggagtgg ttttgaatgt gattctgaga tcagactgac    120

tgagctggaa tcctggcttt atatcttacc agctacacaa ccttggagtc ttagaaattt    180

tttcttttca ataagcagtc atccttactt tccctcaaga tgacaaacag ttcgttcttc    240

tgcccagttt ataaagatct ggagccattc acgtattttt tttatttagt tttccttgtt    300

ggaattattg gaagttgttt tgcaacctgg gcttttatac agaagaatac gaatcacagg    360

tgtgtgagca tctacttaat taatttgctt acagccgatt tcctgcttac tctggcatta    420

ccagtgaaaa ttgttgttga cttgggtgtg gcaccttgga agctgaagat attccactgc    480

caagtaacag cctgcctcat ctatatcaat atgtatttat caattatctt cttagcattt    540

gtcagcattg accgctgtct tcagctgaca cacagctgca agatctaccg aatacaagaa    600

cccggatttg ccaaaatgat atcaaccgtt gtgtggctaa tggtccttct tataatggtg    660

ccaaatatga tgattcccat caaagacatc aaggaaaagt caaatgtggg ttgtatggag    720

tttaaaaagg aatttggaag aaattggcat ttgctgacaa atttcatatg tgtagcaata    780

tttttaaatt tctcagccat cattttaata tccaattgcc ttgtaattcg acagctctac    840

agaaacaaag ataatgaaaa ttacccaaat gtgaaaaagg ctctcatcaa catacttta    900

gtgaccacgg gctacatcat atgctttgtt ccttaccaca ttgtccgaat cccgtatacc    960

ctcagccaga cagaagtcat aactgattgc tcaaccagga tttcactctt caaagccaaa   1020

gaggctacac tgctcctggc tgtgtcgaac ctgtgctttg atcctatcct gtactatcac   1080

ctctcaaaag cattccgctc aaaggtcact gagacttttg cctcacctaa agagaccaag   1140

gctcagaaag aaaaattaag atgtgaaaat aatgcataaa agacaggatt ttttgtgcta   1200
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ccaattctgg ccttactgga ccataaagtt aattatagct ttgaaagata aaaaaaaaaa   1260

aaaagcggcc gc   1272

<210>   2923
<211>   413
<212>   DNA
<213>   Homo sapiens

<400>   2923
tttttttttt tttttgtaga gggtcacatc aatccatagg aaaggaaacc tgcttcttct   60

cacaaaggga taacttttgt tttcctcatg agtcaacttg aaggataact ttaaaaaatt   120

ggtccatgca gcagagtgag actccgtctc aaaaaaaaaa aaaaaaaaaa aaaaaggtcc   180

atgcagaaga ctatcttttt ccaatttgta taagggaact atgtaagttc actgtagctc   240

tgggtatcct caacccacag atctggcagg cagcttgcag cccatcttca gaggagggcc   300

aagtgtccat tcagactcgg gtatttccac actagctgtc tttgagttcc atcaagtaga   360

tagagaactt ctgatccaag ggattttata gagattacaa ccccctcgtg ccg   413

<210>   2924
<211>   474
<212>   DNA
<213>   Homo sapiens

<400>   2924
tttttttttt tgcttcaatt cctttctata caaccgtggt tctcaaccag gggtccttct   60

ggtccccagg ggatgctagg tggtgtctgg gggcatttgt gactgttatg actcagggat   120

gctcctggcg tggagtgggt ggaggccagg gatgctgatc agaaccttgc agtggccagg   180

acaacccccac cccagagaac gacccagccc tgaatgccaa gggggagaga ctctgcctta   240

attatttgga aaaatattgt atctgctccc tgttgacacc agacactaga aaaaattccc   300

gatggggtgg atggcagaaa ccaaggggggg ccccagctcc tgcgattctc ctcctctctc   360

cctccccact cagggtgtgg attacaatgt gtgcagcctc ctggaacctc aggaggacag   420

aggatcatga gacacagagt ttcttgggga tctgtggaat cccctaaccc ccgg   474

<210>   2925
<211>   199
<212>   PRT
<213>   Homo sapiens

<400>   2925

Met Ser Ser Glu Asn Cys Phe Val Ala Glu Asn Ser Ser Leu His Pro
1   5   10   15

Glu Ser Gly Gln Glu Asn Asp Ala Thr Ser Pro His Phe Ser Thr Arg
        20   25   30

His Glu Gly Ser Phe Gln Val Pro Val Leu Cys Ala Val Met Asn Val
        35   40   45

Val Phe Ile Thr Ile Leu Ile Ile Ala Leu Ile Ala Leu Ser Val Gly
        50   55   60

Gln Tyr Asn Cys Pro Gly Gln Tyr Thr Phe Ser Met Pro Ser Asp Ser
65   70   75   80

His Val Ser Ser Cys Ser Glu Asp Trp Val Gly Tyr Gln Arg Lys Cys
                85   90   95

Tyr Phe Ile Ser Thr Val Lys Arg Ser Trp Thr Ser Ala Gln Asn Ala
        100   105   110

Cys Ser Glu His Gly Ala Thr Leu Ala Val Ile Asp Ser Glu Lys Asp
        115   120   125

Met Asn Phe Leu Lys Arg Tyr Ala Gly Arg Glu Glu His Trp Val Gly
        130   135   140

Leu Lys Lys Glu Pro Gly His Pro Trp Lys Trp Ser Asn Gly Lys Glu
145   150   155   160

Phe Asn Asn Trp Phe Asn Val Thr Gly Ser Asp Lys Cys Val Phe Leu
                165   170   175

Lys Asn Thr Glu Val Ser Ser Met Glu Cys Glu Lys Asn Leu Tyr Trp
                180   185   190

Ile Cys Asn Lys Pro Tyr Lys
        195

<210> 2926
<211> 326
<212> PRT
<213> Homo sapiens

<400> 2926

Met Asp Tyr Ser His Gln Thr Ser Leu Val Pro Cys Gly Gln Asp Lys
1   5   10   15

Tyr Ile Ser Lys Asn Glu Leu Leu Leu His Leu Lys Thr Tyr Asn Leu
        20   25   30

Tyr Tyr Glu Gly Gln Asn Leu Gln Leu Arg His Arg Glu Glu Glu Asp
            35   40   45

Glu Phe Ile Val Glu Gly Leu Leu Asn Ile Ser Trp Gly Leu Arg Arg
    50   55   60

Pro Ile Arg Leu Gln Met Gln Asp Asp Asn Glu Arg Ile Arg Pro Pro
65   70   75   80

Pro Ser Ser Ser Ser Trp His Ser Gly Cys Asn Leu Gly Ala Gln Gly
            85   90   95

Thr Thr Leu Lys Pro Leu Thr Val Pro Lys Val Gln Ile Ser Glu Val
            100   105   110

Asp Ala Pro Pro Glu Gly Asp Gln Met Pro Ser Ser Thr Asp Ser Arg
            115   120   125

Gly Leu Lys Pro Leu Gln Glu Asp Thr Pro Gln Leu Met Arg Thr Arg
    130   135   140

Ser Asp Val Gly Val Arg Arg Arg Gly Asn Val Arg Thr Pro Ser Asp
145   150   155   160

Gln Arg Arg Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr
            165   170   175

Asn His Lys Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn
            180   185   190

Val Arg Ile Asn Ser Thr Met Thr Thr Pro Gln Val Leu Lys Leu Leu
    195   200   205

Leu Asn Lys Phe Lys Ile Glu Asn Ser Ala Glu Glu Phe Ala Leu Tyr
    210   .   215   220

Val Val His Thr Ser Gly Glu Lys Gln Lys Leu Lys Ala Thr Asp Tyr
225   230   235   240

Pro Leu Ile Ala Arg Ile Leu Gln Gly Pro Cys Glu Gln Ile Ser Lys
            245   250   255

Val Phe Leu Met Glu Lys Asp Gln Val Glu Glu Val Thr Tyr Asp Val
            260   265   270

```
Ala Gln Tyr Ile Lys Phe Glu Met Pro Val Leu Lys Ser Phe Ile Gln
        275                 280                 285


Lys Leu Gln Glu Glu Glu Asp Arg Glu Val Lys Lys Leu Met Arg Lys
    290                 295                 300


Tyr Thr Val Leu Arg Leu Met Ile Arg Gln Arg Leu Glu Glu Ile Ala
305                 310                 315                 320


Glu Thr Pro Ala Thr Ile
                325



<210> 2927
<211> 364
<212> PRT
<213> Homo sapiens

<400> 2927

Met Pro Leu Leu Leu Leu Leu Pro Leu Leu Trp Ala Gly Ala Leu Ala
1               5                   10                  15


Met Asp Pro Asn Phe Trp Leu Gln Val Gln Glu Ser Val Thr Val Gln
            20                  25                  30


Glu Gly Leu Cys Val Leu Val Pro Cys Thr Phe Phe His Pro Ile Pro
        35                  40                  45


Tyr Tyr Asp Lys Asn Ser Pro Val His Gly Tyr Trp Phe Arg Glu Gly
    50                  55                  60


Ala Ile Ile Ser Gly Asp Ser Pro Val Ala Thr Asn Lys Leu Asp Gln
65                  70                  75                  80


Glu Val Gln Glu Glu Thr Gln Gly Arg Phe Arg Leu Leu Gly Asp Pro
                85                  90                  95


Ser Arg Asn Asn Cys Ser Leu Ser Ile Val Asp Ala Arg Arg Arg Asp
            100                 105                 110


Asn Gly Ser Tyr Phe Phe Arg Met Glu Arg Gly Ser Thr Lys Tyr Ser
            115                 120                 125


Tyr Lys Ser Pro Gln Leu Ser Val His Val Thr Asp Leu Thr His Arg
    130                 135                 140


Pro Lys Ile Leu Ile Pro Gly Thr Leu Glu Pro Gly His Ser Lys Asn
```

145   150   155   160

Leu Thr Cys Ser Val Ser Trp Ala Cys Glu Gln Gly Thr Pro Pro Ile
                165   170   175

Phe Ser Trp Leu Ser Ala Ala Pro Thr Ser Leu Gly Pro Arg Thr Thr
                180   185   190

His Ser Ser Val Leu Ile Ile Thr Pro Arg Pro Gln Asp His Gly Thr
                195   200   205

Asn Leu Thr Cys Gln Val Lys Phe Ala Gly Ala Gly Val Thr Thr Glu
    210   215   220

Arg Thr Ile Gln Leu Asn Val Thr Tyr Val Pro Gln Asn Pro Thr Thr
225   230   235   240

Gly Ile Phe Pro Gly Asp Gly Ser Gly Lys Gln Glu Thr Arg Ala Gly
                245   250   255

Leu Val His Gly Ala Ile Gly Gly Ala Gly Val Thr Ala Leu Leu Ala
                260   265   270

Leu Cys Leu Cys Leu Ile Phe Phe Ile Val Lys Thr His Arg Arg Lys
                275   280   285

Ala Ala Arg Thr Ala Val Gly Ser Asn Asp Thr His Pro Thr Thr Gly
    290   295   300

Ser Ala Ser Pro Lys His Gln Lys Asn Ser Lys Leu His Gly Pro Thr
305   310   315   320

Glu Thr Ser Ser Cys Ser Gly Ala Ala Pro Thr Val Glu Met Asp Glu
                325   330   335

Glu Leu His Tyr Ala Ser Leu Asn Phe His Gly Met Asn Pro Ser Lys
                340   345   350

Asp Thr Ser Thr Glu Tyr Ser Glu Val Arg Thr Gln
                355   360

<210> 2928
<211> 326
<212> PRT
<213> Homo sapiens

<400> 2928

1269

```
Met Asp Tyr Ser His Gln Thr Ser Leu Val Pro Cys Gly Gln Asp Lys
1               5               10              15

Tyr Ile Ser Lys Asn Glu Leu Leu Leu His Leu Lys Thr Tyr Asn Leu
            20              25              30

Tyr Tyr Glu Gly Gln Asn Leu Gln Leu Arg His Arg Glu Glu Glu Asp
        35              40              45

Glu Phe Ile Val Glu Gly Leu Leu Asn Ile Ser Trp Gly Leu Arg Arg
    50              55              60

Pro Ile Arg Leu Gln Met Gln Asp Asp Asn Glu Arg Ile Arg Pro Pro
65              70              75              80

Pro Ser Ser Ser Ser Trp His Ser Gly Cys Asn Leu Gly Ala Gln Gly
            85              90              95

Thr Thr Leu Lys Pro Leu Thr Val Pro Lys Val Gln Ile Ser Glu Val
            100             105             110

Asp Ala Pro Pro Glu Gly Asp Gln Met Pro Ser Ser Thr Asp Ser Arg
        115             120             125

Gly Leu Lys Pro Leu Gln Glu Asp Thr Pro Gln Leu Met Arg Thr Arg
    130             135             140

Ser Asp Val Gly Val Arg Arg Arg Gly Asn Val Arg Thr Pro Ser Asp
145             150             155             160

Gln Arg Arg Ile Arg Arg His Arg Phe Ser Ile Asn Gly His Phe Tyr
            165             170             175

Asn His Lys Thr Ser Val Phe Thr Pro Ala Tyr Gly Ser Val Thr Asn
        180             185             190

Val Arg Ile Asn Ser Thr Met Thr Thr Pro Gln Val Leu Lys Leu Leu
    195             200             205

Leu Asn Lys Phe Lys Ile Glu Asn Ser Ala Glu Glu Phe Ala Leu Tyr
    210             215             220

Val Val His Thr Ser Gly Glu Lys Gln Lys Leu Lys Ala Thr Asp Tyr
225             230             235             240
```

```
Pro Leu Ile Ala Arg Ile Leu Gln Gly Pro Cys Glu Gln Ile Ser Lys
            245             250             255
```

```
Val Phe Leu Met Glu Lys Asp Gln Val Glu Glu Val Thr Tyr Asp Val
            260             265             270
```

```
Ala Gln Tyr Ile Lys Phe Glu Met Pro Val Leu Lys Ser Phe Ile Gln
            275             280             285
```

```
Lys Leu Gln Glu Glu Glu Asp Arg Glu Val Lys Lys Leu Met Arg Lys
            290             295             300
```

```
Tyr Thr Val Leu Arg Leu Met Ile Arg Gln Arg Leu Glu Glu Ile Ala
305             310             315             320
```

```
Glu Thr Pro Ala Thr Ile
                325
```

```
<210>  2929
<211>  1842
<212>  PRT
<213>  Homo sapiens
```

```
<400>  2929
```

```
Leu Pro His Gly Arg Thr Arg Gly Pro Gly Pro Ala Met Ala Pro Trp
1               5               10              15
```

```
Arg Lys Ala Asp Lys Glu Arg His Gly Val Ala Ile Tyr Asn Phe Gln
            20              25              30
```

```
Gly Ser Gly Ala Pro Gln Leu Ser Leu Gln Ile Gly Asp Val Val Arg
            35              40              45
```

```
Ile Gln Glu Thr Cys Gly Asp Trp Tyr Arg Gly Tyr Leu Ile Lys His
            50              55              60
```

```
Lys Met Leu Gln Gly Ile Phe Pro Lys Ser Phe Ile His Ile Lys Glu
65              70              75              80
```

```
Val Thr Val Glu Lys Arg Arg Asn Thr Glu Asn Ile Ile Pro Ala Glu
            85              90              95
```

```
Ile Pro Leu Ala Gln Glu Val Thr Thr Thr Leu Trp Glu Trp Gly Ser
            100             105             110
```

```
Ile Trp Lys Gln Leu Tyr Val Ala Ser Lys Lys Glu Arg Phe Leu Gln
            115             120             125
```

```
Val Gln Ser Met Met Tyr Asp Leu Met Glu Trp Arg Ser Gln Leu Leu
    130                 135             140

Ser Gly Thr Leu Pro Lys Asp Glu Leu Lys Glu Leu Lys Gln Lys Val
145                 150             155                 160

Thr Ser Lys Ile Asp Tyr Gly Asn Lys Ile Leu Glu Leu Asp Leu Ile
                165             170             175

Val Arg Asp Glu Asp Gly Asn Ile Leu Asp Pro Asp Asn Thr Ser Val
            180             185             190

Ile Ser Leu Phe His Ala His Glu Glu Ala Thr Asp Lys Ile Thr Glu
        195             200             205

Arg Ile Lys Glu Glu Met Ser Lys Asp Gln Pro Asp Tyr Ala Met Tyr
    210             215             220

Ser Arg Ile Ser Ser Ser Pro Thr His Ser Leu Tyr Val Phe Val Arg
225             230             235                 240

Asn Phe Val Cys Arg Ile Gly Glu Asp Ala Glu Leu Phe Met Ser Leu
                245             250             255

Tyr Asp Pro Asn Lys Gln Thr Val Ile Ser Glu Asn Tyr Leu Val Arg
            260             265             270

Trp Gly Ser Arg Gly Phe Pro Lys Glu Ile Glu Met Leu Asn Asn Leu
        275             280             285

Lys Val Val Phe Thr Asp Leu Gly Asn Lys Asp Leu Asn Arg Asp Lys
    290             295             300

Ile Tyr Leu Ile Cys Gln Ile Val Arg Val Gly Lys Met Asp Leu Lys
305             310             315                 320

Asp Thr Gly Ala Lys Lys Cys Thr Gln Gly Leu Arg Arg Pro Phe Gly
                325             330             335

Val Ala Val Met Asp Ile Thr Asp Ile Ile Lys Gly Lys Ala Glu Ser
            340             345             350

Asp Glu Glu Lys Gln His Phe Ile Pro Phe His Pro Val Thr Ala Glu
        355             360             365
```

```
Asn Asp Phe Leu His Ser Leu Leu Gly Lys Val Ile Ala Ser Lys Gly
    370               375               380

Asp Ser Gly Gly Gln Gly Leu Trp Val Thr Met Lys Met Leu Val Gly
385               390               395               400

Asp Ile Ile Gln Ile Arg Lys Asp Tyr Pro His Leu Val Asp Arg Thr
            405               410               415

Thr Val Val Ala Arg Lys Leu Gly Phe Pro Glu Ile Ile Met Pro Gly
            420               425               430

Asp Val Arg Asn Asp Ile Tyr Ile Thr Leu Leu Gln Gly Asp Phe Asp
            435               440               445

Lys Tyr Asn Lys Thr Thr Gln Arg Asn Val Glu Val Ile Met Cys Val
    450               455               460

Cys Ala Glu Asp Gly Lys Thr Leu Pro Asn Ala Ile Cys Val Gly Ala
465               470               475               480

Gly Asp Lys Pro Met Asn Glu Tyr Arg Ser Val Val Tyr Tyr Gln Val
            485               490               495

Lys Gln Pro Arg Trp Met Glu Thr Val Lys Val Ala Val Pro Ile Glu
            500               505               510

Asp Met Gln Arg Ile His Leu Arg Phe Met Phe Arg His Arg Ser Ser
    515               520               525

Leu Glu Ser Lys Asp Lys Gly Glu Lys Asn Phe Ala Met Ser Tyr Val
    530               535               540

Lys Leu Met Lys Glu Asp Gly Thr Thr Leu His Asp Gly Phe His Asp
545               550               555               560

Leu Val Val Leu Lys Gly Asp Ser Lys Lys Met Glu Asp Ala Ser Ala
            565               570               575

Tyr Leu Thr Leu Pro Ser Tyr Arg His His Val Glu Asn Lys Gly Ala
            580               585               590

Thr Leu Ser Arg Ser Ser Ser Ser Val Gly Gly Leu Ser Val Ser Ser
    595               600               605
```

Arg Asp Val Phe Ser Ile Ser Thr Leu Val Cys Ser Thr Lys Leu Thr
    610   615   620

Gln Asn Val Gly Leu Leu Gly Leu Leu Lys Trp Arg Met Lys Pro Gln
625   630   635   640

Leu Leu Gln Glu Asn Leu Glu Lys Leu Lys Ile Val Asp Gly Glu Glu
            645   650   655

Val Val Lys Phe Leu Gln Asp Thr Leu Asp Ala Leu Phe Asn Ile Met
            660   665   670

Met Glu His Ser Gln Ser Asp Glu Tyr Asp Ile Leu Val Phe Asp Ala
        675   680   685

Leu Ile Tyr Ile Ile Gly Leu Ile Ala Asp Arg Lys Phe Gln His Phe
    690   695   700

Asn Thr Val Leu Glu Ala Tyr Ile Gln Gln His Phe Ser Ala Thr Leu
705   710   715   720

Ala Tyr Lys Lys Leu Met Thr Val Leu Lys Thr Tyr Leu Asp Thr Ser
            725   730   735

Ser Arg Gly Glu Gln Cys Glu Pro Ile Leu Arg Thr Leu Lys Ala Leu
            740   745   750

Glu Tyr Val Phe Lys Phe Ile Val Arg Ser Arg Thr Leu Phe Ser Gln
        755   760   765

Leu Tyr Glu Gly Lys Glu Gln Met Glu Phe Glu Glu Ser Met Arg Arg
    770   775   780

Leu Phe Glu Ser Ile Asn Asn Leu Met Lys Ser Gln Tyr Lys Thr Thr
785   790   795   800

Ile Leu Leu Gln Val Ala Ala Leu Lys Tyr Ile Pro Ser Val Leu His
            805   810   815

Asp Val Glu Met Val Phe Asp Ala Lys Leu Leu Ser Gln Leu Leu Tyr
        820   825   830

Glu Phe Tyr Thr Cys Ile Pro Pro Val Lys Leu Gln Lys Gln Lys Val
    835   840   845

Gln Ser Met Asn Glu Ile Val Gln Ser Asn Leu Phe Lys Lys Gln Glu

                850   855   860

Cys Arg Asp Ile Leu Leu Pro Val Ile Thr Lys Glu Leu Lys Glu Leu
865   870   875   880

Leu Glu Gln Lys Asp Asp Met Gln His Gln Val Leu Glu Arg Lys Tyr
                885   890   895

Cys Val Glu Leu Leu Asn Ser Ile Leu Glu Val Leu Ser Tyr Gln Asp
            900   905   910

Ala Ala Phe Thr Tyr His His Ile Gln Glu Ile Met Val Gln Leu Leu
            915   920   925

Arg Thr Val Asn Arg Thr Val Ile Thr Met Gly Arg Asp His Ile Leu
    930   935   940

Ile Ser His Phe Val Ala Cys Met Thr Ala Ile Leu Asn Gln Met Gly
945   950   955   960

Asp Gln His Tyr Ser Phe Tyr Ile Glu Thr Phe Gln Thr Ser Ser Glu
                965   970   975

Leu Val Asp Phe Leu Met Glu Thr Phe Ile Met Phe Lys Asp Leu Ile
            980   985   990

Gly Lys Asn Val Tyr Pro Gly Asp Trp Met Ala Met Ser Met Val Gln
            995   1000   1005

Asn Arg Val Phe Leu Arg Ala Ile Asn Lys Phe Ala Glu Thr Met
    1010   1015   1020

Asn Gln Lys Phe Leu Glu His Thr Asn Phe Glu Phe Gln Leu Trp
    1025   1030   1035

Asn Asn Tyr Phe His Leu Ala Val Ala Phe Ile Thr Gln Asp Ser
    1040   1045   1050

Leu Gln Leu Glu Gln Phe Ser His Ala Lys Tyr Asn Lys Ile Leu
    1055   1060   1065

Asn Lys Tyr Gly Asp Met Arg Arg Leu Ile Gly Phe Ser Ile Arg
    1070   1075   1080

Asp Met Trp Tyr Lys Leu Gly Gln Asn Lys Ile Cys Phe Ile Pro
    1085   1090   1095

```
Gly Met  Val Gly Pro Ile Leu  Glu Met Thr Leu Ile  Pro Glu Ala
    1100                 1105              1110

Glu Leu  Arg Lys Ala Thr Ile  Pro Ile Phe Phe Asp  Met Met Leu
    1115                 1120              1125

Cys Glu  Tyr Gln Arg Ser Gly  Asp Phe Lys Lys Phe  Glu Asn Glu
    1130                 1135              1140

Ile Ile  Leu Lys Leu Asp His  Glu Val Glu Gly Gly  Arg Gly Asp
    1145                 1150              1155

Glu Gln  Tyr Met Gln Leu Leu  Glu Ser Ile Leu Met  Glu Cys Ala
    1160                 1165              1170

Ala Glu  His Pro Thr Ile Ala  Lys Ser Val Glu Asn  Phe Val Asn
    1175                 1180              1185

Leu Val  Lys Gly Leu Leu Glu  Lys Leu Leu Asp Tyr  Arg Gly Val
    1190                 1195              1200

Met Thr  Asp Glu Ser Lys Asp  Asn Arg Met Ser Cys  Thr Val Asn
    1205                 1210              1215

Leu Leu  Asn Phe Tyr Lys Asp  Asn Asn Arg Glu Glu  Met Tyr Ile
    1220                 1225              1230

Arg Tyr  Leu Tyr Lys Leu Arg  Asp Leu His Leu Asp  Cys Asp Asn
    1235                 1240              1245

Tyr Thr  Glu Ala Ala Tyr Thr  Leu Leu Leu His Thr  Trp Leu Leu
    1250                 1255              1260

Lys Trp  Ser Asp Glu Gln Cys  Ala Ser Gln Val Met  Gln Thr Gly
    1265                 1270              1275

Gln Gln  His Pro Gln Thr His  Arg Gln Leu Lys Glu  Thr Leu Tyr
    1280                 1285              1290

Glu Thr  Ile Ile Gly Tyr Phe  Asp Lys Gly Lys Met  Trp Glu Glu
    1295                 1300              1305

Ala Ile  Ser Leu Cys Lys Glu  Leu Ala Glu Gln Tyr  Glu Met Glu
    1310                 1315              1320
```

Ile Phe Asp Tyr Glu Leu Leu Ser Gln Asn Leu Ile Gln Gln Ala
    1325   1330   1335

Lys Phe Tyr Glu Ser Ile Met Lys Ile Leu Arg Pro Lys Pro Asp
    1340   1345   1350

Tyr Phe Ala Val Gly Tyr Tyr Gly Gln Gly Phe Pro Ser Phe Leu
    1355   1360   1365

Arg Asn Lys Val Phe Ile Tyr Arg Gly Lys Glu Tyr Glu Arg Arg
    1370   1375   1380

Glu Asp Phe Gln Met Gln Leu Met Thr Gln Phe Pro Asn Ala Glu
    1385   1390   1395

Lys Met Asn Thr Thr Ser Ala Pro Gly Asp Asp Val Lys Asn Ala
    1400   1405   1410

Pro Gly Gln Tyr Ile Gln Cys Phe Thr Val Gln Pro Val Leu Asp
    1415   1420   1425

Glu His Pro Arg Phe Lys Asn Lys Pro Val Pro Asp Gln Ile Ile
    1430   1435   1440

Asn Phe Tyr Lys Ser Asn Tyr Val Gln Arg Phe His Tyr Ser Arg
    1445   1450   1455

Pro Val Arg Arg Gly Thr Val Asp Pro Glu Asn Glu Phe Ala Ser
    1460   1465   1470

Met Trp Ile Glu Arg Thr Ser Phe Val Thr Ala Tyr Lys Leu Pro
    1475   1480   1485

Gly Ile Leu Arg Trp Phe Glu Val Val His Met Ser Gln Thr Thr
    1490   1495   1500

Ile Ser Pro Leu Glu Asn Ala Ile Glu Thr Met Ser Thr Ala Asn
    1505   1510   1515

Glu Lys Ile Leu Met Met Ile Asn Gln Tyr Gln Ser Asp Glu Thr
    1520   1525   1530

Leu Pro Ile Asn Pro Leu Ser Met Leu Leu Asn Gly Ile Val Asp
    1535   1540   1545

Pro Ala Val Met Gly Gly Phe Ala Lys Tyr Glu Lys Ala Phe Phe
    1550   1555   1560

Thr Glu Glu Tyr Val Arg Asp His Pro Glu Asp Gln Asp Lys Leu
    1565   1570   1575

Thr His Leu Lys Asp Leu Ile Ala Trp Gln Ile Pro Phe Leu Gly
    1580   1585   1590

Ala Gly Ile Lys Ile His Glu Lys Arg Val Ser Asp Asn Leu Arg
    1595   1600   1605

Pro Phe His Asp Arg Met Glu Glu Cys Phe Lys Asn Leu Lys Met
    1610   1615   1620

Lys Val Glu Lys Glu Tyr Gly Val Arg Glu Met Pro Asp Phe Asp
    1625   1630   1635

Asp Arg Arg Val Gly Arg Pro Arg Ser Met Leu Arg Ser Tyr Arg
    1640   1645   1650

Gln Met Ser Ile Ile Ser Leu Ala Ser Met Asn Ser Asp Cys Ser
    1655   1660   1665

Thr Pro Ser Lys Pro Thr Ser Glu Ser Phe Asp Leu Glu Leu Ala
    1670   1675   1680

Ser Pro Lys Thr Pro Arg Val Glu Gln Glu Glu Pro Ile Ser Pro
    1685   1690   1695

Gly Ser Thr Leu Pro Glu Val Lys Leu Arg Arg Ser Lys Lys Arg
    1700   1705   1710

Thr Lys Arg Ser Ser Val Val Phe Ala Asp Glu Lys Ala Ala Ala
    1715   1720   1725

Glu Ser Asp Leu Lys Arg Leu Ser Arg Lys His Glu Phe Met Ser
    1730   1735   1740

Asp Thr Asn Leu Ser Glu His Ala Ala Ile Pro Leu Lys Ala Ser
    1745   1750   1755

Val Leu Ser Gln Met Ser Phe Ala Ser Gln Ser Met Pro Thr Ile
    1760   1765   1770

Pro Ala Leu Ala Leu Ser Val Ala Gly Ile Pro Gly Leu Asp Glu

```
        1775                    1780                    1785


Ala Asn  Thr Ser Pro Arg Leu  Ser Gln Thr Phe Leu  Gln Leu Ser
    1790                    1795                  1800


Asp Gly  Asp Lys Lys Thr Leu  Thr Arg Lys Lys Val  Asn Gln Phe
    1805                    1810                  1815


Phe Lys  Thr Met Leu Ala Ser  Lys Ser Ala Glu Glu  Gly Lys Gln
    1820                    1825                  1830


Ile Pro  Asp Ser Leu Ser Thr  Asp Leu
    1835                    1840


<210>  2930
<211>  386
<212>  PRT
<213>  Homo sapiens

<400>  2930

Met Glu Glu Leu Asp Ala Leu Leu Glu Glu Leu Glu Arg Ser Thr Leu
1             5                10                15


Gln Asp Ser Asp Glu Tyr Ser Asn Pro Ala Pro Leu Pro Leu Asp Gln
            20              25                30


His Ser Arg Lys Glu Thr Asn Leu Asp Glu Thr Ser Glu Ile Leu Ser
        35                40                45


Ile Gln Asp Asn Thr Ser Pro Leu Pro Ala Gln Leu Val Tyr Thr Thr
    50                55                60


Asn Ile Gln Glu Leu Asn Val Tyr Ser Glu Ala Gln Glu Pro Lys Glu
65                70                75                80


Ser Pro Pro Pro Ser Lys Thr Ser Ala Ala Ala Gln Leu Asp Glu Leu
                85                90                95


Met Ala His Leu Thr Glu Met Gln Ala Lys Val Ala Val Arg Ala Asp
            100               105               110


Ala Gly Lys Lys His Leu Pro Asp Lys Gln Asp His Lys Ala Ser Leu
        115               120               125


Asp Ser Met Leu Gly Gly Leu Glu Gln Glu Leu Gln Asp Leu Gly Ile
    130               135               140
```

```
Ala Thr Val Pro Lys Gly His Cys Ala Ser Cys Gln Lys Pro Ile Ala
145             150             155             160


Gly Lys Val Ile His Ala Leu Gly Gln Ser Trp His Pro Glu His Phe
                165             170             175


Val Cys Thr His Cys Lys Glu Glu Ile Gly Ser Ser Pro Phe Phe Glu
            180             185             190


Arg Ser Gly Leu Ala Tyr Cys Pro Asn Asp Tyr His Gln Leu Phe Ser
        195             200             205


Pro Arg Cys Ala Tyr Cys Ala Ala Pro Ile Leu Asp Lys Val Leu Thr
    210             215             220


Ala Met Asn Gln Thr Trp His Pro Glu His Phe Phe Cys Ser His Cys
225             230             235             240


Gly Glu Val Phe Gly Ala Glu Gly Phe His Glu Lys Asp Lys Lys Pro
            245             250             255


Tyr Cys Arg Lys Asp Phe Leu Ala Met Phe Ser Pro Lys Cys Gly Gly
        260             265             270


Cys Asn Arg Pro Val Leu Glu Asn Tyr Leu Ser Ala Met Asp Thr Val
    275             280             285


Trp His Pro Glu Cys Phe Val Cys Gly Asp Cys Phe Thr Ser Phe Ser
    290             295             300


Thr Gly Ser Phe Phe Glu Leu Asp Gly Arg Pro Phe Cys Glu Leu His
305             310             315             320


Tyr His His Arg Arg Gly Thr Leu Cys His Gly Cys Gly Gln Pro Ile
            325             330             335


Thr Gly Arg Cys Ile Ser Ala Met Gly Tyr Lys Phe His Pro Glu His
        340             345             350


Phe Val Cys Ala Phe Cys Leu Thr Gln Leu Ser Lys Gly Ile Phe Arg
        355             360             365


Glu Gln Asn Asp Lys Thr Tyr Cys Gln Pro Cys Phe Asn Lys Leu Phe
    370             375             380
```

Pro Leu
385

<210> 2931
<211> 368
<212> PRT
<213> Homo sapiens

<400> 2931

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1   5   10   15

Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
                20   25   30

Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
                35   40   45

Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
        50   55   60

Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65   70   75   80

Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
                85   90   95

Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
                100   105   110

Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
            115   120   125

Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
        130   135   140

Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145   150   155   160

Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
                165   170   175

Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
            180   185   190

His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
            195   200   205

```
Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220

Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240

Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255

Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
                260                 265                 270

Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
                275                 280                 285

Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300

Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320

Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335

Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
                340                 345                 350

Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
                355                 360                 365
```

```
<210>  2932
<211>  359
<212>  PRT
<213>  Homo sapiens

<400>  2932
```

```
Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala Pro
1               5                   10                  15

Leu Lys Lys Ser Ile Ser Ser Arg Leu Gly Gln Asp Pro Gly Ala Asp
                20                  25                  30

Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro Ala Val Leu
    35                  40                  45
```

Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly Asp Lys Ala Ala
    50   55   60

Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg Ala Val Thr Ser Pro
65   70   75   80

Ala Val Gly Arg Ile Leu Pro Cys Arg Thr Thr Cys Leu Arg Tyr Leu
            85   90   95

Leu Leu Gly Leu Leu Leu Thr Cys Leu Leu Leu Gly Val Thr Ala Ile
            100   105   110

Cys Leu Gly Val Arg Tyr Leu Gln Val Ser Gln Gln Leu Gln Gln Thr
            115   120   125

Asn Arg Val Leu Glu Val Thr Asn Ser Ser Leu Arg Gln Gln Leu Arg
    130   135   140

Leu Lys Ile Thr Gln Leu Gly Gln Ser Ala Glu Asp Leu Gln Gly Ser
145   150   155   160

Arg Arg Glu Leu Ala Gln Ser Gln Glu Ala Leu Gln Val Glu Gln Arg
            165   170   175

Ala His Gln Ala Ala Glu Gly Gln Leu Gln Ala Cys Gln Ala Asp Arg
            180   185   190

Gln Lys Thr Lys Glu Thr Leu Gln Ser Glu Glu Gln Gln Arg Arg Ala
    195   200   205

Leu Glu Gln Lys Leu Ser Asn Met Glu Asn Arg Leu Lys Pro Phe Phe
    210   215   220

Thr Cys Gly Ser Ala Asp Thr Cys Cys Pro Ser Gly Trp Ile Met His
225   230   235   240

Gln Lys Ser Cys Phe Tyr Ile Ser Leu Thr Ser Lys Asn Trp Gln Glu
            245   250   255

Ser Gln Lys Gln Cys Glu Thr Leu Ser Ser Lys Leu Ala Thr Phe Ser
            260   265   270

Glu Ile Tyr Pro Gln Ser His Ser Tyr Tyr Phe Leu Asn Ser Leu Leu
    275   280   285

Pro Asn Gly Gly Ser Gly Asn Ser Tyr Trp Thr Gly Leu Ser Ser Asn

1283

```
      290                    295                    300
```

```
Lys Asp Trp Lys Leu Thr Asp Asp Thr Gln Arg Thr Arg Thr Tyr Ala
305             310             315             320
```

```
Gln Ser Ser Lys Cys Asn Lys Val His Lys Thr Trp Ser Trp Trp Thr
            325             330             335
```

```
Leu Glu Ser Glu Ser Cys Arg Ser Ser Leu Pro Tyr Ile Cys Glu Met
            340             345             350
```

```
Thr Ala Phe Arg Phe Pro Asp
        355
```

```
<210>   2933
<211>   266
<212>   PRT
<213>   Homo sapiens
```

```
<400>   2933
```

```
Met Arg Val Thr Leu Ala Thr Ile Ala Trp Met Val Ser Phe Val Ser
1               5               10              15
```

```
Asn Tyr Ser His Thr Ala Asn Ile Leu Pro Asp Ile Glu Asn Glu Asp
            20              25              30
```

```
Phe Ile Lys Asp Cys Val Arg Ile His Asn Lys Phe Arg Ser Glu Val
        35              40              45
```

```
Lys Pro Thr Ala Ser Asp Met Leu Tyr Met Thr Trp Asp Pro Ala Leu
    50              55              60
```

```
Ala Gln Ile Ala Lys Ala Trp Ala Ser Asn Cys Gln Phe Ser His Asn
65              70              75              80
```

```
Thr Arg Leu Lys Pro Pro His Lys Leu His Pro Asn Phe Thr Ser Leu
            85              90              95
```

```
Gly Glu Asn Ile Trp Thr Gly Ser Val Pro Ile Phe Ser Val Ser Ser
            100             105             110
```

```
Ala Ile Thr Asn Trp Tyr Asp Glu Ile Gln Asp Tyr Asp Phe Lys Thr
        115             120             125
```

```
Arg Ile Cys Lys Lys Val Cys Gly His Tyr Thr Gln Val Val Trp Ala
        130             135             140
```

```
Asp Ser Tyr Lys Val Gly Cys Ala Val Gln Phe Cys Pro Lys Val Ser
145             150             155             160


Gly Phe Asp Ala Leu Ser Asn Gly Ala His Phe Ile Cys Asn Tyr Gly
                165             170             175


Pro Gly Gly Asn Tyr Pro Thr Trp Pro Tyr Lys Arg Gly Ala Thr Cys
            180             185             190


Ser Ala Cys Pro Asn Asn Asp Lys Cys Leu Asp Asn Leu Cys Val Asn
            195             200             205


Arg Gln Arg Asp Gln Val Lys Arg Tyr Tyr Ser Val Val Tyr Pro Gly
    210             215             220


Trp Pro Ile Tyr Pro Arg Asn Arg Tyr Thr Ser Leu Phe Leu Ile Val
225             230             235             240


Asn Ser Val Ile Leu Ile Leu Ser Val Ile Ile Thr Ile Leu Val Gln
                245             250             255


Leu Lys Tyr Pro Asn Leu Val Leu Leu Asp
            260             265
```

```
<210>   2934
<211>   1429
<212>   PRT
<213>   Homo sapiens

<400>   2934
```

```
Met Ala Gly Gly Ala Trp Gly Arg Leu Ala Cys Tyr Leu Glu Phe Leu
1               5               10              15


Lys Lys Glu Glu Leu Lys Glu Phe Gln Leu Leu Leu Ala Asn Lys Ala
            20              25              30


His Ser Arg Ser Ser Ser Gly Glu Thr Pro Ala Gln Pro Glu Lys Thr
            35              40              45


Ser Gly Met Glu Val Ala Ser Tyr Leu Val Ala Gln Tyr Gly Glu Gln
    50              55              60


Arg Ala Trp Asp Leu Ala Leu His Thr Trp Glu Gln Met Gly Leu Arg
65              70              75              80


Ser Leu Cys Ala Gln Ala Gln Glu Gly Ala Gly His Ser Pro Ser Phe
```

```
              85                    90                    95


Pro Tyr Ser Pro Ser Glu Pro His Leu Gly Ser Pro Ser Gln Pro Thr
            100               105               110


Ser Thr Ala Val Leu Met Pro Trp Ile His Glu Leu Pro Ala Gly Cys
            115               120               125


Thr Gln Gly Ser Glu Arg Arg Val Leu Arg Gln Leu Pro Asp Thr Ser
            130               135               140


Gly Arg Arg Trp Arg Glu Ile Ser Ala Ser Leu Leu Tyr Gln Ala Leu
145               150               155               160


Pro Ser Ser Pro Asp His Glu Ser Pro Ser Gln Glu Ser Pro Asn Ala
                165               170               175


Pro Thr Ser Thr Ala Val Leu Gly Ser Trp Gly Ser Pro Pro Gln Pro
            180               185               190


Ser Leu Ala Pro Arg Glu Gln Glu Ala Pro Gly Thr Gln Trp Pro Leu
            195               200               205


Asp Glu Thr Ser Gly Ile Tyr Tyr Thr Glu Ile Arg Glu Arg Glu Arg
    210               215               220


Glu Lys Ser Glu Lys Gly Arg Pro Pro Trp Ala Ala Val Val Gly Thr
225               230               235               240


Pro Pro Gln Ala His Thr Ser Leu Gln Pro His His His Pro Trp Glu
                245               250               255


Pro Ser Val Arg Glu Ser Leu Cys Ser Thr Trp Pro Trp Lys Asn Glu
                260               265               270


Asp Phe Asn Gln Lys Phe Thr Gln Leu Leu Leu Leu Gln Arg Pro His
            275               280               285


Pro Arg Ser Gln Asp Pro Leu Val Lys Arg Ser Trp Pro Asp Tyr Val
    290               295               300


Glu Glu Asn Arg Gly His Leu Ile Glu Ile Arg Asp Leu Phe Gly Pro
305               310               315               320


Gly Leu Asp Thr Gln Glu Pro Arg Ile Val Ile Leu Gln Gly Ala Ala
                325               330               335
```

```
Gly Ile Gly Lys Ser Thr Leu Ala Arg Gln Val Lys Glu Ala Trp Gly
            340                 345                 350

Arg Gly Gln Leu Tyr Gly Asp Arg Phe Gln His Val Phe Tyr Phe Ser
            355                 360                 365

Cys Arg Glu Leu Ala Gln Ser Lys Val Val Ser Leu Ala Glu Leu Ile
    370                 375                 380

Gly Lys Asp Gly Thr Ala Thr Pro Ala Pro Ile Arg Gln Ile Leu Ser
385                 390                 395                 400

Arg Pro Glu Arg Leu Leu Phe Ile Leu Asp Gly Val Asp Glu Pro Gly
                405                 410                 415

Trp Val Leu Gln Glu Pro Ser Ser Glu Leu Cys Leu His Trp Ser Gln
            420                 425                 430

Pro Gln Pro Ala Asp Ala Leu Leu Gly Ser Leu Leu Gly Lys Thr Ile
            435                 440                 445

Leu Pro Glu Ala Ser Phe Leu Ile Thr Ala Arg Thr Thr Ala Leu Gln
    450                 455                 460

Asn Leu Ile Pro Ser Leu Glu Gln Ala Arg Trp Val Glu Val Leu Gly
465                 470                 475                 480

Phe Ser Glu Ser Ser Arg Lys Glu Tyr Phe Tyr Arg Tyr Phe Thr Asp
            485                 490                 495

Glu Arg Gln Ala Ile Arg Ala Phe Arg Leu Val Lys Ser Asn Lys Glu
            500                 505                 510

Leu Trp Ala Leu Cys Leu Val Pro Trp Val Ser Trp Leu Ala Cys Thr
            515                 520                 525

Cys Leu Met Gln Gln Met Lys Arg Lys Glu Lys Leu Thr Leu Thr Ser
    530                 535                 540

Lys Thr Thr Thr Thr Leu Cys Leu His Tyr Leu Ala Gln Ala Leu Gln
545                 550                 555                 560

Ala Gln Pro Leu Gly Pro Gln Leu Arg Asp Leu Cys Ser Leu Ala Ala
            565                 570                 575
```

Glu Gly Ile Trp Gln Lys Lys Thr Leu Phe Ser Pro Asp Asp Leu Arg
        580   585   590

Lys His Gly Leu Asp Gly Ala Ile Ile Ser Thr Phe Leu Lys Met Gly
        595   600   605

Ile Leu Gln Glu His Pro Ile Pro Leu Ser Tyr Ser Phe Ile His Leu
        610   615   620

Cys Phe Gln Glu Phe Phe Ala Ala Met Ser Tyr Val Leu Glu Asp Glu
625   630   635   640

Lys Gly Arg Gly Lys His Ser Asn Cys Ile Ile Asp Leu Glu Lys Thr
            645   650   655

Leu Glu Ala Tyr Gly Ile His Gly Leu Phe Gly Ala Ser Thr Thr Arg
            660   665   670

Phe Leu Leu Gly Leu Leu Ser Asp Glu Gly Glu Arg Glu Met Glu Asn
        675   680   685

Ile Phe His Cys Arg Leu Ser Gln Gly Arg Asn Leu Met Gln Trp Val
        690   695   700

Pro Ser Leu Gln Leu Leu Leu Gln Pro His Ser Leu Glu Ser Leu His
705   710   715   720

Cys Leu Tyr Glu Thr Arg Asn Lys Thr Phe Leu Thr Gln Val Met Ala
            725   730   735

His Phe Glu Glu Met Gly Met Cys Val Glu Thr Asp Met Glu Leu Leu
            740   745   750

Val Cys Thr Phe Cys Ile Lys Phe Ser Arg His Val Lys Lys Leu Gln
            755   760   765

Leu Ile Glu Gly Arg Gln His Arg Ser Thr Trp Ser Pro Thr Met Val
        770   775   780

Val Leu Phe Arg Trp Val Pro Val Thr Asp Ala Tyr Trp Gln Ile Leu
785   790   795   800

Phe Ser Val Leu Lys Val Thr Arg Asn Leu Lys Glu Leu Asp Leu Ser
            805   810   815

1288

```
Gly Asn Ser Leu Ser His Ser Ala Val Lys Ser Leu Cys Lys Thr Leu
        820             825             830

Arg Arg Pro Arg Cys Leu Leu Glu Thr Leu Arg Leu Ala Gly Cys Gly
        835             840             845

Leu Thr Ala Glu Asp Cys Lys Asp Leu Ala Phe Gly Leu Arg Ala Asn
    850             855             860

Gln Thr Leu Thr Glu Leu Asp Leu Ser Phe Asn Val Leu Thr Asp Ala
865             870             875             880

Gly Ala Lys His Leu Cys Gln Arg Leu Arg Gln Pro Ser Cys Lys Leu
        885             890             895

Gln Arg Leu Gln Leu Val Ser Cys Gly Leu Thr Ser Asp Cys Cys Gln
        900             905             910

Asp Leu Ala Ser Val Leu Ser Ala Ser Pro Ser Leu Lys Glu Leu Asp
        915             920             925

Leu Gln Gln Asn Asn Leu Asp Asp Val Gly Val Arg Leu Leu Cys Glu
    930             935             940

Gly Leu Arg His Pro Ala Cys Lys Leu Ile Arg Leu Gly Leu Asp Gln
945             950             955             960

Thr Thr Leu Ser Asp Glu Met Arg Gln Glu Leu Arg Ala Leu Glu Gln
            965             970             975

Glu Lys Pro Gln Leu Leu Ile Phe Ser Arg Arg Lys Pro Ser Val Met
        980             985             990

Thr Pro Thr Glu Gly Leu Asp Thr  Gly Glu Met Ser Asn  Ser Thr Ser
        995             1000            1005

Ser Leu  Lys Arg Gln Arg Leu  Gly Ser Glu Arg Ala  Ala Ser His
    1010            1015            1020

Val Ala  Gln Ala Asn Leu Lys  Leu Leu Asp Val Ser  Lys Ile Phe
    1025            1030            1035

Pro Ile  Ala Glu Ile Ala Glu  Glu Ser Ser Pro Glu  Val Val Pro
    1040            1045            1050

Val Glu  Leu Leu Cys Val Pro  Ser Pro Ala Ser Gln  Gly Asp Leu
```

```
        1055                    1060                    1065


His Thr Lys Pro Leu Gly Thr Asp Asp Asp Phe Trp Gly Pro Thr
    1070                1075                1080


Gly Pro Val Ala Thr Glu Val Val Asp Lys Glu Lys Asn Leu Tyr
    1085                1090                1095


Arg Val His Phe Pro Val Ala Gly Ser Tyr Arg Trp Pro Asn Thr
    1100                1105                1110


Gly Leu Cys Phe Val Met Arg Glu Ala Val Thr Val Glu Ile Glu
    1115                1120                1125


Phe Cys Val Trp Asp Gln Phe Leu Gly Glu Ile Asn Pro Gln His
    1130                1135                1140


Ser Trp Met Val Ala Gly Pro Leu Leu Asp Ile Lys Ala Glu Pro
    1145                1150                1155


Gly Ala Val Glu Ala Val His Leu Pro His Phe Val Ala Leu Gln
    1160                1165                1170


Gly Gly His Val Asp Thr Ser Leu Phe Gln Met Ala His Phe Lys
    1175                1180                1185


Glu Glu Gly Met Leu Leu Glu Lys Pro Ala Arg Val Glu Leu His
    1190                1195                1200


His Ile Val Leu Glu Asn Pro Ser Phe Ser Pro Leu Gly Val Leu
    1205                1210                1215


Leu Lys Met Ile His Asn Ala Leu Arg Phe Ile Pro Val Thr Ser
    1220                1225                1230


Val Val Leu Leu Tyr His Arg Val His Pro Glu Glu Val Thr Phe
    1235                1240                1245


His Leu Tyr Leu Ile Pro Ser Asp Cys Ser Ile Arg Lys Glu Leu
    1250                1255                1260


Glu Leu Cys Tyr Arg Ser Pro Gly Glu Asp Gln Leu Phe Ser Glu
    1265                1270                1275


Phe Tyr Val Gly His Leu Gly Ser Gly Ile Arg Leu Gln Val Lys
    1280                1285                1290
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Asp Lys Lys Asp Glu Thr Leu Val Trp Glu Ala Leu Val Lys Pro
    1295             1300             1305


Gly Asp Leu Met Pro Ala Thr Thr Leu Ile Pro Pro Ala Arg Ile
    1310             1315             1320


Ala Val Pro Ser Pro Leu Asp Ala Pro Gln Leu Leu His Phe Val
    1325             1330             1335


Asp Gln Tyr Arg Glu Gln Leu Ile Ala Arg Val Thr Ser Val Glu
    1340             1345             1350


Val Val Leu Asp Lys Leu His Gly Gln Val Leu Ser Gln Glu Gln
    1355             1360             1365


Tyr Glu Arg Val Leu Ala Glu Asn Thr Arg Pro Ser Gln Met Arg
    1370             1375             1380


Lys Leu Phe Ser Leu Ser Gln Ser Trp Asp Arg Lys Cys Lys Asp
    1385             1390             1395


Gly Leu Tyr Gln Ala Leu Lys Glu Thr His Pro His Leu Ile Met
    1400             1405             1410


Glu Leu Trp Glu Lys Gly Ser Lys Lys Gly Leu Leu Pro Leu Ser
    1415             1420             1425


Ser
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<210>  2935
<211>  352
<212>  PRT
<213>  Homo sapiens

<400>  2935

Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1               5               10              15


Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
                20              25              30


Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
        35              40              45
```

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
    50   55   60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65   70   75   80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
                85   90   95

Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
                100   105   110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
    115   120   125

Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130   135   140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145   150   155   160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
                165   170   175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
                180   185   190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
    195   200   205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
    210   215   220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225   230   235   240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
                245   250   255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
                260   265   270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
    275   280   285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe

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            290                    295                    300
```

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305   310   315   320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
                325   330   335

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
                340   345   350

<210> 2936
<211> 248
<212> PRT
<213> Homo sapiens

<400> 2936

Met Leu Ser Thr Val Gly Ser Phe Leu Gln Asp Leu Gln Asn Glu Asp
1   5   10   15

Lys Gly Ile Lys Thr Ala Ala Ile Phe Thr Ala Asp Gly Asn Met Ile
                20   25   30

Ser Ala Ser Thr Leu Met Asp Ile Leu Leu Met Asn Asp Phe Lys Leu
        35   40   45

Val Ile Asn Lys Ile Ala Tyr Asp Val Gln Cys Pro Lys Arg Glu Lys
        50   55   60

Pro Ser Asn Glu His Thr Ala Glu Met Glu His Met Lys Ser Leu Val
65   70   75   80

His Arg Leu Phe Thr Ile Leu His Leu Glu Glu Ser Gln Lys Lys Arg
                85   90   95

Glu His His Leu Leu Glu Lys Ile Asp His Leu Lys Glu Gln Leu Gln
                100   105   110

Pro Leu Glu Gln Val Lys Ala Gly Ile Glu Ala His Ser Glu Ala Lys
            115   120   125

Thr Ser Gly Leu Leu Trp Ala Gly Leu Ala Leu Leu Ser Ile Gln Gly
            130   135   140

Gly Ala Leu Ala Trp Leu Thr Trp Trp Val Tyr Ser Trp Asp Ile Met
145   150   155   160

Glu Pro Val Thr Tyr Phe Ile Thr Phe Ala Asn Ser Met Val Phe Phe
                165   170   175

Ala Tyr Phe Ile Val Thr Arg Gln Asp Tyr Thr Tyr Ser Ala Val Lys
            180   185   190

Ser Arg Gln Phe Leu Gln Phe Phe His Lys Lys Ser Lys Gln Gln His
        195   200   205

Phe Asp Val Gln Gln Tyr Asn Lys Leu Lys Glu Asp Leu Ala Lys Ala
    210   215   220

Lys Glu Ser Leu Lys Gln Ala Arg His Ser Leu Cys Leu Gln Met Gln
225   230   235   240

Val Glu Glu Leu Asn Glu Lys Asn
                245

<210>   2937
<211>   790
<212>   PRT
<213>   Homo sapiens

<400>   2937

Met Ala Glu Gln Val Leu Pro Gln Ala Leu Tyr Leu Ser Asn Met Arg
1   5   10   15

Lys Ala Val Lys Ile Arg Glu Arg Thr Pro Glu Asp Ile Phe Lys Pro
            20   25   30

Thr Asn Gly Ile Ile His His Phe Lys Thr Met His Arg Tyr Thr Leu
        35   40   45

Glu Met Phe Arg Thr Cys Gln Phe Cys Pro Gln Phe Arg Glu Ile Ile
    50   55   60

His Lys Ala Leu Ile Asp Arg Asn Ile Gln Ala Thr Leu Glu Ser Gln
65   70   75   80

Lys Lys Leu Asn Trp Cys Arg Glu Val Arg Lys Leu Val Ala Leu Lys
            85   90   95

Thr Asn Gly Asp Gly Asn Cys Leu Met His Ala Thr Ser Gln Tyr Met
            100   105   110

Trp Gly Val Gln Asp Thr Asp Leu Val Leu Arg Lys Ala Leu Phe Ser

            115   120   125

Thr Leu Lys Glu Thr Asp Thr Arg Asn Phe Lys Phe Arg Trp Gln Leu
    130   135   140

Glu Ser Leu Lys Ser Gln Glu Phe Val Glu Thr Gly Leu Cys Tyr Asp
145   150   155   160

Thr Arg Asn Trp Asn Asp Glu Trp Asp Asn Leu Ile Lys Met Ala Ser
              165   170   175

Thr Asp Thr Pro Met Ala Arg Ser Gly Leu Gln Tyr Asn Ser Leu Glu
          180   185   190

Glu Ile His Ile Phe Val Leu Cys Asn Ile Leu Arg Arg Pro Ile Ile
          195   200   205

Val Ile Ser Asp Lys Met Leu Arg Ser Leu Glu Ser Gly Ser Asn Phe
    210   215   220

Ala Pro Leu Lys Val Gly Gly Ile Tyr Leu Pro Leu His Trp Pro Ala
225   230   235   240

Gln Glu Cys Tyr Arg Tyr Pro Ile Val Leu Gly Tyr Asp Ser His His
              245   250   255

Phe Val Pro Leu Val Thr Leu Lys Asp Ser Gly Pro Glu Ile Arg Ala
          260   265   270

Val Pro Leu Val Asn Arg Asp Arg Gly Arg Phe Glu Asp Leu Lys Val
    275   280   285

His Phe Leu Thr Asp Pro Glu Asn Glu Met Lys Glu Lys Leu Leu Lys
    290   295   300

Glu Tyr Leu Met Val Ile Glu Ile Pro Val Gln Gly Trp Asp His Gly
305   310   315   320

Thr Thr His Leu Ile Asn Ala Ala Lys Leu Asp Glu Ala Asn Leu Pro
              325   330   335

Lys Glu Ile Asn Leu Val Asp Asp Tyr Phe Glu Leu Val Gln His Glu
              340   345   350

Tyr Lys Lys Trp Gln Glu Asn Ser Glu Gln Gly Arg Arg Glu Gly His
          355   360   365

```
Ala Gln Asn Pro Met Glu Pro Ser Val Pro Gln Leu Ser Leu Met Asp
    370             375             380

Val Lys Cys Glu Thr Pro Asn Cys Pro Phe Phe Met Ser Val Asn Thr
385             390             395             400

Gln Pro Leu Cys His Glu Cys Ser Glu Arg Arg Gln Lys Asn Gln Asn
            405             410             415

Lys Leu Pro Lys Leu Asn Ser Lys Pro Gly Pro Glu Gly Leu Pro Gly
            420             425             430

Met Ala Leu Gly Ala Ser Arg Gly Glu Ala Tyr Glu Pro Leu Ala Trp
    435             440             445

Asn Pro Glu Glu Ser Thr Gly Gly Pro His Ser Ala Pro Pro Thr Ala
    450             455             460

Pro Ser Pro Phe Leu Phe Ser Glu Thr Thr Ala Met Lys Cys Arg Ser
465             470             475             480

Pro Gly Cys Pro Phe Thr Leu Asn Val Gln His Asn Gly Phe Cys Glu
            485             490             495

Arg Cys His Asn Ala Arg Gln Leu His Ala Ser His Ala Pro Asp His
            500             505             510

Thr Arg His Leu Asp Pro Gly Lys Cys Gln Ala Cys Leu Gln Asp Val
            515             520             525

Thr Arg Thr Phe Asn Gly Ile Cys Ser Thr Cys Phe Lys Arg Thr Thr
    530             535             540

Ala Glu Ala Ser Ser Ser Leu Ser Thr Ser Leu Pro Pro Ser Cys His
545             550             555             560

Gln Arg Ser Lys Ser Asp Pro Ser Arg Leu Val Arg Ser Pro Ser Pro
            565             570             575

His Ser Cys His Arg Ala Gly Asn Asp Ala Pro Ala Gly Cys Leu Ser
            580             585             590

Gln Ala Ala Arg Thr Pro Gly Asp Arg Thr Gly Thr Ser Lys Cys Arg
    595             600             605
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```
Lys Ala Gly Cys Val Tyr Phe Gly Thr Pro Glu Asn Lys Gly Phe Cys
    610             615             620

Thr Leu Cys Phe Ile Glu Tyr Arg Glu Asn Lys His Phe Ala Ala Ala
625             630             635             640

Ser Gly Lys Val Ser Pro Thr Ala Ser Arg Phe Gln Asn Thr Ile Pro
            645             650             655

Cys Leu Gly Arg Glu Cys Gly Thr Leu Gly Ser Thr Met Phe Glu Gly
            660             665             670

Tyr Cys Gln Lys Cys Phe Ile Glu Ala Gln Asn Gln Arg Phe His Glu
        675             680             685

Ala Lys Arg Thr Glu Glu Gln Leu Arg Ser Ser Gln Arg Arg Asp Val
    690             695             700

Pro Arg Thr Thr Gln Ser Thr Ser Arg Pro Lys Cys Ala Arg Ala Ser
705             710             715             720

Cys Lys Asn Ile Leu Ala Cys Arg Ser Glu Glu Leu Cys Met Glu Cys
            725             730             735

Gln His Pro Asn Gln Arg Met Gly Pro Gly Ala His Arg Gly Glu Pro
            740             745             750

Ala Pro Glu Asp Pro Pro Lys Gln Arg Cys Arg Ala Pro Ala Cys Asp
        755             760             765

His Phe Gly Asn Ala Lys Cys Asn Gly Tyr Cys Asn Glu Cys Phe Gln
    770             775             780

Phe Lys Gln Met Tyr Gly
785             790


<210> 2938
<211> 206
<212> PRT
<213> Homo sapiens

<400> 2938

Met Ala Leu Pro Cys Thr Leu Gly Leu Gly Met Leu Leu Ala Leu Pro
1               5               10              15


Gly Ala Leu Gly Ser Gly Gly Ser Ala Glu Asp Ser Val Gly Ser Ser
```

                    20   25   30

Ser Val Thr Val Val Leu Leu Leu Leu Leu Leu Leu Leu Ala Thr
        35   40   45

Gly Leu Ala Leu Ala Trp Arg Arg Leu Ser Arg Asp Ser Gly Gly Tyr
    50   55   60

Tyr His Pro Ala Arg Leu Gly Ala Ala Leu Trp Gly Arg Thr Arg Arg
65   70   75   80

Leu Leu Trp Ala Ser Pro Pro Gly Arg Trp Leu Gln Ala Arg Ala Glu
                85   90   95

Leu Gly Ser Thr Asp Asn Asp Leu Glu Arg Gln Glu Asp Glu Gln Asp
            100   105   110

Thr Asp Tyr Asp His Val Ala Asp Gly Gly Leu Gln Ala Asp Pro Gly
            115   120   125

Glu Gly Glu Gln Gln Cys Gly Glu Ala Ser Ser Pro Glu Gln Val Pro
    130   135   140

Val Arg Ala Glu Glu Ala Arg Asp Ser Asp Thr Glu Gly Asp Leu Val
145   150   155   160

Leu Gly Ser Pro Gly Pro Ala Ser Ala Gly Gly Ser Ala Glu Ala Leu
                165   170   175

Leu Ser Asp Leu His Ala Phe Ala Gly Ser Ala Ala Trp Asp Asp Ser
            180   185   190

Ala Arg Ala Ala Gly Gly Gln Gly Leu His Val Thr Ala Leu
        195   200   205

<210> 2939
<211> 718
<212> PRT
<213> Homo sapiens

<400> 2939

Met Ile Val Asp Lys Leu Leu Asp Asp Ser Arg Gly Gly Glu Gly Leu
1   5   10   15

Arg Asp Ala Ala Gly Gly Cys Gly Leu Met Thr Ser Pro Leu Asn Leu
            20   25   30

```
Ser Tyr Phe Tyr Gly Ala Ser Pro Pro Ala Ala Ala Pro Gly Ala Cys
        35              40              45

Asp Ala Ser Cys Ser Val Leu Gly Pro Ser Ala Pro Gly Ser Pro Gly
    50              55              60

Ser Asp Ser Ser Asp Phe Ser Ser Ala Ser Ser Val Ser Ser Cys Gly
65              70              75              80

Ala Val Glu Ser Arg Ser Arg Gly Gly Ala Arg Ala Glu Arg Gln Pro
            85              90              95

Val Glu Pro His Met Gly Val Gly Arg Gln Gln Arg Gly Pro Phe Gln
            100             105             110

Gly Val Arg Val Lys Asn Ser Val Lys Glu Leu Leu Leu His Ile Arg
        115             120             125

Ser His Lys Gln Lys Ala Ser Gly Gln Ala Val Asp Asp Phe Lys Thr
    130             135             140

Gln Gly Val Asn Ile Glu Gln Phe Arg Glu Leu Lys Asn Thr Val Ser
145             150             155             160

Tyr Ser Gly Lys Arg Lys Gly Pro Asp Ser Leu Ser Asp Gly Pro Ala
            165             170             175

Cys Lys Arg Pro Ala Leu Leu His Ser Gln Phe Leu Thr Pro Pro Gln
        180             185             190

Thr Pro Thr Pro Gly Glu Ser Met Glu Asp Val His Leu Asn Glu Pro
        195             200             205

Lys Gln Glu Ser Ser Ala Asp Leu Leu Gln Asn Ile Ile Asn Ile Lys
    210             215             220

Asn Glu Cys Ser Pro Val Ser Leu Asn Thr Val Gln Val Ser Trp Leu
225             230             235             240

Asn Pro Val Val Val Pro Gln Ser Ser Pro Ala Glu Gln Cys Gln Asp
            245             250             255

Phe His Gly Gly Gln Val Phe Ser Pro Pro Gln Lys Cys Gln Pro Phe
            260             265             270
```

Gln Val Arg Gly Ser Gln Gln Met Ile Asp Gln Ala Ser Leu Tyr Gln
        275   280   285

Tyr Ser Pro Gln Asn Gln His Val Glu Gln Gln Pro His Tyr Thr His
        290   295   300

Lys Pro Thr Leu Glu Tyr Ser Pro Phe Pro Ile Pro Pro Gln Ser Pro
305   310   315   320

Ala Tyr Glu Pro Asn Leu Phe Asp Gly Pro Glu Ser Gln Phe Cys Pro
                325   330   335

Asn Gln Ser Leu Val Ser Leu Leu Gly Asp Gln Arg Glu Ser Glu Asn
            340   345   350

Ile Ala Asn Pro Met Gln Thr Ser Ser Ser Val Gln Gln Gln Asn Asp
        355   360   365

Ala His Leu His Ser Phe Ser Met Met Pro Ser Ser Ala Cys Glu Ala
    370   375   380

Met Val Gly His Glu Met Ala Ser Asp Ser Ser Asn Thr Ser Leu Pro
385   390   395   400

Phe Ser Asn Met Gly Asn Pro Met Asn Thr Thr Gln Leu Gly Lys Ser
                405   410   415

Leu Phe Gln Trp Gln Val Glu Gln Glu Glu Ser Lys Leu Ala Asn Ile
            420   425   430

Ser Gln Asp Gln Phe Leu Ser Lys Asp Ala Asp Gly Asp Thr Phe Leu
        435   440   445

His Ile Ala Val Ala Gln Gly Arg Arg Ala Leu Ser Tyr Val Leu Ala
    450   455   460

Arg Lys Met Asn Ala Leu His Met Leu Asp Ile Lys Glu His Asn Gly
465   470   475   480

Gln Ser Ala Phe Gln Val Ala Val Ala Ala Asn Gln His Leu Ile Val
                485   490   495

Gln Asp Leu Val Asn Ile Gly Ala Gln Val Asn Thr Thr Asp Cys Trp
            500   505   510

Gly Arg Thr Pro Leu His Val Cys Ala Glu Lys Gly His Ser Gln Val

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              515                    520                      525


Leu Gln Ala Ile Gln Lys Gly Ala Val Gly Ser Asn Gln Phe Val Asp
        530               535            540


Leu Glu Ala Thr Asn Tyr Asp Gly Leu Thr Pro Leu His Cys Ala Val
545               550            555                      560


Ile Ala His Asn Ala Val Val His Glu Leu Gln Arg Asn Gln Gln Pro
                565            570            575


His Ser Pro Glu Val Gln Glu Leu Leu Leu Lys Asn Lys Ser Leu Val
            580            585            590


Asp Thr Ile Lys Cys Leu Ile Gln Met Gly Ala Ala Val Glu Ala Lys
        595            600            605


Asp Arg Lys Ser Gly Arg Thr Ala Leu His Leu Ala Ala Glu Glu Ala
    610            615            620


Asn Leu Glu Leu Ile Arg Leu Phe Leu Glu Leu Pro Ser Cys Leu Ser
625            630            635                      640


Phe Val Asn Ala Lys Ala Tyr Asn Gly Asn Thr Ala Leu His Val Ala
            645            650            655


Ala Ser Leu Gln Tyr Arg Leu Thr Gln Leu Asp Ala Val Arg Leu Leu
        660            665            670


Met Arg Lys Gly Ala Asp Pro Ser Thr Arg Asn Leu Glu Asn Glu Gln
        675            680            685


Pro Val His Leu Val Pro Asp Gly Pro Val Gly Glu Gln Ile Arg Arg
    690            695            700


Ile Leu Lys Gly Lys Ser Ile Gln Gln Arg Ala Pro Pro Tyr
705            710            715


<210>  2940
<211>  247
<212>  PRT
<213>  Homo sapiens

<400>  2940

Met Gln Pro Ile Leu Leu Leu Leu Ala Phe Leu Leu Leu Pro Arg Ala
1              5                  10                  15
```

Asp Ala Gly Glu Ile Ile Gly Gly His Glu Ala Lys Pro His Ser Arg
              20   25   30

Pro Tyr Met Ala Tyr Leu Met Ile Trp Asp Gln Lys Ser Leu Lys Arg
        35   40   45

Cys Gly Gly Phe Leu Ile Gln Asp Asp Phe Val Leu Thr Ala Ala His
    50   55   60

Cys Trp Gly Ser Ser Ile Asn Val Thr Leu Gly Ala His Asn Ile Lys
65   70   75   80

Glu Gln Glu Pro Thr Gln Gln Phe Ile Pro Val Lys Arg Pro Ile Pro
            85   90   95

His Pro Ala Tyr Asn Pro Lys Asn Phe Ser Asn Asp Ile Met Leu Leu
            100   105   110

Gln Leu Glu Arg Lys Ala Lys Arg Thr Arg Ala Val Gln Pro Leu Arg
    115   120   125

Leu Pro Ser Asn Lys Ala Gln Val Lys Pro Gly Gln Thr Cys Ser Val
    130   135   140

Ala Gly Trp Gly Gln Thr Ala Pro Leu Gly Lys His Ser His Thr Leu
145   150   155   160

Gln Glu Val Lys Met Thr Val Gln Glu Asp Arg Lys Cys Glu Ser Asp
            165   170   175

Leu Arg His Tyr Tyr Asp Ser Thr Ile Glu Leu Cys Val Gly Asp Pro
        180   185   190

Glu Ile Lys Lys Thr Ser Phe Lys Gly Asp Ser Gly Gly Pro Leu Val
    195   200   205

Cys Asn Lys Val Ala Gln Gly Ile Val Ser Tyr Gly Arg Asn Asn Gly
    210   215   220

Met Pro Pro Arg Ala Cys Thr Lys Val Ser Ser Phe Val His Trp Ile
225   230   235   240

Lys Lys Thr Met Lys Arg Tyr
            245

<210> 2941
<211> 191
<212> PRT
<213> Homo sapiens

<400> 2941

Met His Asp Ser Asn Asn Val Glu Lys Asp Ile Thr Pro Ser Glu Leu
1   5   10   15

Pro Ala Asn Pro Gly Cys Leu His Ser Lys Glu His Ser Ile Lys Ala
            20   25   30

Thr Leu Ile Trp Arg Leu Phe Phe Leu Ile Met Phe Leu Thr Ile Ile
        35   40   45

Val Cys Gly Met Val Ala Ala Leu Ser Ala Ile Arg Ala Asn Cys His
    50   55   60

Gln Glu Pro Ser Val Cys Leu Gln Ala Ala Cys Pro Glu Ser Trp Ile
65   70   75   80

Gly Phe Gln Arg Lys Cys Phe Tyr Phe Ser Asp Asp Thr Lys Asn Trp
            85   90   95

Thr Ser Ser Gln Arg Phe Cys Asp Ser Gln Asp Ala Asp Leu Ala Gln
            100   105   110

Val Glu Ser Phe Gln Glu Leu Asn Phe Leu Leu Arg Tyr Lys Gly Pro
        115   120   125

Ser Asp His Trp Ile Gly Leu Ser Arg Glu Gln Gly Gln Pro Trp Lys
    130   135   140

Trp Ile Asn Gly Thr Glu Trp Thr Arg Gln Phe Pro Ile Leu Gly Ala
145   150   155   160

Gly Glu Cys Ala Tyr Leu Asn Asp Lys Gly Ala Ser Ser Ala Arg His
            165   170   175

Tyr Thr Glu Arg Lys Trp Ile Cys Ser Lys Ser Asp Ile His Val
            180   185   190

<210> 2942
<211> 441
<212> PRT
<213> Homo sapiens

<400> 2942

```
Met Glu Ile Arg Leu Asp Thr Leu Ser Ala Ser Leu Gly Arg Ser Ser
1             5               10              15

Thr Leu Asn Asp Cys Asn Leu Glu Asp Lys Leu Ala Trp Tyr Glu Gly
        20              25              30

Glu Ala Tyr Met Trp His His Trp Lys Pro Phe Pro Glu Asn Pro Leu
        35              40              45

Trp Thr Cys Leu Asp Phe Gln Ile Ala Gln Val Gly Pro Trp Asp Tyr
50              55              60

Cys Ser Ser Cys Ile Arg His Thr Arg Leu Lys Ser Ser Cys Ser Asp
65              70              75              80

Met Asp Leu Leu His Ser Trp Arg Ser Ser Ser Phe Gly Asn Phe Asp
            85              90              95

Arg Phe Arg Asn Asn Ser Leu Ser Lys Pro Asp Asp Ser Thr Glu Ala
        100             105             110

His Glu Gly Asp Pro Thr Asn Gly Ser Gly Glu Gln Ser Lys Thr Ser
        115             120             125

Asn Asn Gly Gly Gly Leu Gly Lys Lys Met Arg Ala Ile Ser Trp Thr
    130             135             140

Met Lys Lys Lys Val Gly Lys Lys Tyr Ile Lys Ala Leu Ser Glu Glu
145             150             155             160

Lys Asp Glu Glu Asp Gly Glu Asn Ala His Pro Tyr Arg Asn Ser Asp
            165             170             175

Pro Val Ile Gly Thr His Thr Glu Lys Val Ser Leu Lys Ala Ser Asp
        180             185             190

Ser Met Asp Ser Leu Tyr Ser Gly Gln Ser Ser Ser Ser Gly Ile Thr
        195             200             205

Ser Cys Ser Asp Gly Thr Ser Asn Arg Asp Ser Phe Arg Leu Asp Asp
    210             215             220

Asp Gly Pro Tyr Ser Gly Pro Phe Cys Gly Arg Ala Arg Val His Thr
225             230             235             240
```

1304

Asp Phe Thr Pro Ser Pro Tyr Asp Thr Asp Ser Leu Lys Ile Lys Lys
            245   250   255

Gly Asp Ile Ile Asp Ile Ile Cys Lys Thr Pro Met Gly Met Trp Thr
            260   265   270

Gly Met Leu Asn Asn Lys Val Gly Asn Phe Lys Phe Ile Tyr Val Asp
            275   280   285

Val Ile Ser Glu Glu Glu Ala Ala Pro Lys Lys Ile Lys Ala Asn Arg
    290   295   300

Arg Ser Asn Ser Lys Lys Ser Lys Thr Leu Gln Glu Phe Leu Glu Arg
305   310   315   320

Ile His Leu Gln Glu Tyr Thr Ser Thr Leu Leu Leu Asn Gly Tyr Glu
            325   330   335

Thr Leu Glu Asp Leu Lys Asp Ile Lys Glu Ser His Leu Ile Glu Leu
            340   345   350

Asn Ile Glu Asn Pro Asp Asp Arg Arg Arg Leu Leu Ser Ala Ala Glu
            355   360   365

Asn Phe Leu Glu Glu Glu Ile Ile Gln Glu Gln Glu Asn Glu Pro Glu
    370   375   380

Pro Leu Ser Leu Ser Ser Asp Ile Ser Leu Asn Lys Ser Gln Leu Asp
385   390   395   400

Asp Cys Pro Arg Asp Ser Gly Cys Tyr Ile Ser Ser Gly Asn Ser Asp
            405   410   415

Asn Gly Lys Glu Asp Leu Glu Ser Glu Asn Leu Ser Asp Met Val His
            420   425   430

Lys Ile Ile Ile Thr Glu Pro Ser Asp
            435   440

<210> 2943
<211> 564
<212> PRT
<213> Homo sapiens

<400> 2943

Met Lys Glu His Gly Gly Thr Phe Ser Ser Thr Gly Ile Ser Gly Gly
1   5   10   15

Ser Gly Asp Ser Ala Met Asp Ser Leu Gln Pro Leu Gln Pro Asn Tyr
        20   25   30

Met Pro Val Cys Leu Phe Ala Glu Glu Ser Tyr Gln Lys Leu Ala Met
        35   40   45

Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Ile
    50   55   60

Gln Thr Tyr Arg Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg
65   70   75   80

Met Leu Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly
            85   90   95

Asn Gln Val Ser Glu Tyr Ile Ser Asn Thr Phe Leu Asp Lys Gln Asn
            100   105   110

Asp Val Glu Ile Pro Ser Pro Thr Gln Lys Asp Arg Glu Lys Lys Lys
            115   120   125

Lys Gln Gln Leu Met Thr Gln Ile Ser Gly Val Lys Lys Leu Met His
    130   135   140

Ser Ser Ser Leu Asn Asn Thr Ser Ile Ser Arg Phe Gly Val Asn Thr
145   150   155   160

Glu Asn Glu Asp His Leu Ala Lys Glu Leu Glu Asp Leu Asn Lys Trp
            165   170   175

Gly Leu Asn Ile Phe Asn Val Ala Gly Tyr Ser His Asn Arg Pro Leu
            180   185   190

Thr Cys Ile Met Tyr Ala Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr
    195   200   205

Phe Arg Ile Ser Ser Asp Thr Phe Ile Thr Tyr Met Met Thr Leu Glu
    210   215   220

Asp His Tyr His Ser Asp Val Ala Tyr His Asn Ser Leu His Ala Ala
225   230   235   240

Asp Val Ala Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Asp
            245   250   255

1306

```
Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ala Ala
            260             265             270


Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn
            275             280             285


Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Glu Ser Val Leu Glu
        290             295             300


Asn His His Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu His Cys
305             310             315             320


Asp Ile Phe Met Asn Leu Thr Lys Lys Gln Arg Gln Thr Leu Arg Lys
            325             330             335


Met Val Ile Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Ser
            340             345             350


Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser
            355             360             365


Ser Gly Val Leu Leu Leu Asp Asn Tyr Thr Asp Arg Ile Gln Val Leu
        370             375             380


Arg Asn Met Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Ser Leu
385             390             395             400


Glu Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Gln
            405             410             415


Gln Gly Asp Lys Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys
            420             425             430


Asp Lys His Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp
            435             440             445


Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val Gln Pro
    450             455             460


Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Asn Trp Tyr
465             470             475             480


Gln Ser Met Ile Pro Gln Ser Pro Ser Pro Pro Leu Asp Glu Gln Asn
            485             490             495
```

Arg Asp Cys Gln Gly Leu Met Glu Lys Phe Gln Phe Glu Leu Thr Leu
          500   505   510

Asp Glu Glu Asp Ser Glu Gly Pro Glu Lys Glu Gly Glu Gly His Ser
          515   520   525

Tyr Phe Ser Ser Thr Lys Thr Leu Cys Val Ile Asp Pro Glu Asn Arg
          530   535   540

Asp Ser Leu Gly Glu Thr Asp Ile Asp Ile Ala Thr Glu Asp Lys Ser
545   550   555   560

Pro Val Asp Thr

<210> 2944
<211> 91
<212> PRT
<213> Homo sapiens

<400> 2944

Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1   5   10   15

Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
          20   25   30

Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
          35   40   45

Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val Phe
          50   55   60

Val Thr Arg Lys Asn Arg Gln Val Cys Ala Asn Pro Glu Lys Lys Trp
65   70   75   80

Val Arg Glu Tyr Ile Asn Ser Leu Glu Met Ser
                85   90

<210> 2945
<211> 461
<212> PRT
<213> Homo sapiens

<400> 2945

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1   5   10   15

```
Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
         20              25              30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
         35              40              45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
    50              55              60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65              70              75              80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
             85              90              95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
         100             105             110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
         115             120             125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
    130             135             140

Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
145             150             155             160

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
             165             170             175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
         180             185             190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
         195             200             205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210             215             220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225             230             235             240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
             245             250             255
```

```
Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
            260             265             270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
        275             280             285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
    290             295             300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305             310             315             320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
            325             330             335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
            340             345             350

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
        355             360             365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
370             375             380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385             390             395             400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
            405             410             415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
            420             425             430

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
        435             440             445

Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
    450             455             460
```

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<210>  2946
<211>  823
<212>  PRT
<213>  Homo sapiens

<400>  2946

Met Ser Arg Arg Lys Gln Gly Asn Pro Gln His Leu Ser Gln Arg Glu
1               5               10              15
```

Leu Ile Thr Pro Glu Ala Asp His Val Glu Ala Ala Ile Leu Glu Glu
            20   25   30

Asp Glu Gly Leu Glu Ile Glu Glu Pro Ser Gly Leu Gly Leu Met Val
            35   40   45

Gly Gly Pro Asp Pro Asp Leu Leu Thr Cys Gly Gln Cys Gln Met Asn
            50   55   60

Phe Pro Leu Gly Asp Ile Leu Val Phe Ile Glu His Lys Arg Lys Gln
65   70   75   80

Cys Gly Gly Ser Leu Gly Ala Cys Tyr Asp Lys Ala Leu Asp Lys Asp
                85   90   95

Ser Pro Pro Pro Ser Ser Arg Ser Glu Leu Arg Lys Val Ser Glu Pro
            100   105   110

Val Glu Ile Gly Ile Gln Val Thr Pro Asp Glu Asp Asp His Leu Leu
            115   120   125

Ser Pro Thr Lys Gly Ile Cys Pro Lys Gln Glu Asn Ile Ala Gly Lys
            130   135   140

Asp Glu Pro Ser Ser Tyr Ile Cys Thr Thr Cys Lys Gln Pro Phe Asn
145   150   155   160

Ser Ala Trp Phe Leu Leu Gln His Ala Gln Asn Thr His Gly Phe Arg
            165   170   175

Ile Tyr Leu Glu Pro Gly Pro Ala Ser Ser Ser Leu Thr Pro Arg Leu
            180   185   190

Thr Ile Pro Pro Pro Leu Gly Pro Glu Ala Val Ala Gln Ser Pro Leu
            195   200   205

Met Asn Phe Leu Gly Asp Ser Asn Pro Phe Asn Leu Leu Arg Met Thr
            210   215   220

Gly Pro Ile Leu Arg Asp His Pro Gly Phe Gly Glu Gly Arg Leu Pro
225   230   235   240

Gly Thr Pro Pro Leu Phe Ser Pro Pro Pro Arg His His Leu Asp Pro
            245   250   255

1311

```
His Arg Leu Ser Ala Glu Glu Met Gly Leu Val Ala Gln His Pro Ser
             260                     265                 270

Ala Phe Asp Arg Val Met Arg Leu Asn Pro Met Ala Ile Asp Ser Pro
         275                 280                 285

Ala Met Asp Phe Ser Arg Arg Leu Arg Glu Leu Ala Gly Asn Ser Ser
         290                 295                 300

Thr Pro Pro Pro Val Ser Pro Gly Arg Gly Asn Pro Met His Arg Leu
305                 310                 315                 320

Leu Asn Pro Phe Gln Pro Ser Pro Lys Ser Pro Phe Leu Ser Thr Pro
             325                 330                 335

Pro Leu Pro Pro Met Pro Pro Gly Gly Thr Pro Pro Pro Gln Pro Pro
             340                 345                 350

Ala Lys Ser Lys Ser Cys Glu Phe Cys Gly Lys Thr Phe Lys Phe Gln
         355                 360                 365

Ser Asn Leu Ile Val His Arg Arg Ser His Thr Gly Glu Lys Pro Tyr
         370                 375                 380

Lys Cys Gln Leu Cys Asp His Ala Cys Ser Gln Ala Ser Lys Leu Lys
385                 390                 395                 400

Arg His Met Lys Thr His Met His Lys Ala Gly Ser Leu Ala Gly Arg
             405                 410                 415

Ser Asp Asp Gly Leu Ser Ala Ala Ser Ser Pro Glu Pro Gly Thr Ser
         420                 425                 430

Glu Leu Ala Gly Glu Gly Leu Lys Ala Ala Asp Gly Asp Phe Arg His
         435                 440                 445

His Glu Ser Asp Pro Ser Leu Gly His Glu Pro Glu Glu Glu Asp Glu
    450                 455                 460

Glu Glu Glu Glu Glu Glu Glu Glu Leu Leu Leu Glu Asn Glu Ser Arg
465                 470                 475                 480

Pro Glu Ser Ser Phe Ser Met Asp Ser Glu Leu Ser Arg Asn Arg Glu
             485                 490                 495
```

1312

```
Asn Gly Gly Gly Gly Val Pro Gly Val Pro Gly Ala Gly Gly Gly Ala
            500             505             510

Ala Lys Ala Leu Ala Asp Glu Lys Ala Leu Val Leu Gly Lys Val Met
            515             520             525

Glu Asn Val Gly Leu Gly Ala Leu Pro Gln Tyr Gly Glu Leu Leu Ala
    530             535             540

Asp Lys Gln Lys Arg Gly Ala Phe Leu Lys Arg Ala Ala Gly Gly Gly
545             550             555             560

Asp Ala Gly Asp Asp Asp Asp Ala Gly Gly Cys Gly Asp Ala Gly Ala
            565             570             575

Gly Gly Ala Val Asn Gly Arg Gly Gly Gly Phe Ala Pro Gly Thr Glu
            580             585             590

Pro Phe Pro Gly Leu Phe Pro Arg Lys Pro Ala Pro Leu Pro Ser Pro
        595             600             605

Gly Leu Asn Ser Ala Ala Lys Arg Ile Lys Val Glu Lys Asp Leu Glu
    610             615             620

Leu Pro Pro Ala Ala Leu Ile Pro Ser Glu Asn Val Tyr Ser Gln Trp
625             630             635             640

Leu Val Gly Tyr Ala Ala Ser Arg His Phe Met Lys Asp Pro Phe Leu
            645             650             655

Gly Phe Thr Asp Ala Arg Gln Ser Pro Phe Ala Thr Ser Ser Glu His
            660             665             670

Ser Ser Glu Asn Gly Ser Leu Arg Phe Ser Thr Pro Pro Gly Asp Leu
    675             680             685

Leu Asp Gly Gly Leu Ser Gly Arg Ser Gly Thr Ala Ser Gly Gly Ser
    690             695             700

Thr Pro His Leu Gly Gly Pro Gly Pro Gly Arg Pro Ser Ser Lys Glu
705             710             715             720

Gly Arg Arg Ser Asp Thr Cys Glu Tyr Cys Gly Lys Val Phe Lys Asn
            725             730             735

Cys Ser Asn Leu Thr Val His Arg Arg Ser His Thr Gly Glu Arg Pro
```

```
              740                745                750
```

Tyr Lys Cys Glu Leu Cys Asn Tyr Ala Cys Ala Gln Ser Ser Lys Leu
         755   760   765

Thr Arg His Met Lys Thr His Gly Gln Ile Gly Lys Glu Val Tyr Arg
    770   775   780

Cys Asp Ile Cys Gln Met Pro Phe Ser Val Tyr Ser Thr Leu Glu Lys
785   ,   790   795   800

His Met Lys Lys Trp His Gly Glu His Leu Leu Thr Asn Asp Val Lys
                 805   810   815

Ile Glu Gln Ala Glu Arg Ser
              820

<210> 2947
<211> 441
<212> PRT
<213> Homo sapiens

<400> 2947

Met Val Pro Pro Lys Leu His Val Leu Phe Cys Leu Cys Gly Cys Leu
1   5   10   15

Ala Val Val Tyr Pro Phe Asp Trp Gln Tyr Ile Asn Pro Val Ala His
         20   25   30

Met Lys Ser Ser Ala Trp Val Asn Lys Ile Gln Val Leu Met Ala Ala
    35   40   45

Ala Ser Phe Gly Gln Thr Lys Ile Pro Arg Gly Asn Gly Pro Tyr Ser
    50   55   60

Val Gly Cys Thr Asp Leu Met Phe Asp His Thr Asn Lys Gly Thr Phe
65   70   75   80

Leu Arg Leu Tyr Tyr Pro Ser Gln Asp Asn Asp Arg Leu Asp Thr Leu
              85   90   95

Trp Ile Pro Asn Lys Glu Tyr Phe Trp Gly Leu Ser Lys Phe Leu Gly
         100   105   110

Thr His Trp Leu Met Gly Asn Ile Leu Arg Leu Leu Phe Gly Ser Met
         115   120   125

Thr Thr Pro Ala Asn Trp Asn Ser Pro Leu Arg Pro Gly Glu Lys Tyr
    130   135   140

Pro Leu Val Val Phe Ser His Gly Leu Gly Ala Phe Arg Thr Leu Tyr
145   150   155   160

Ser Ala Ile Gly Ile Asp Leu Ala Ser His Gly Phe Ile Val Ala Ala
                165   170   175

Val Glu His Arg Asp Arg Ser Ala Ser Ala Thr Tyr Tyr Phe Lys Asp
            180   185   190

Gln Ser Ala Ala Glu Ile Gly Asp Lys Ser Trp Leu Tyr Leu Arg Thr
        195   200   205

Leu Lys Gln Glu Glu Glu Thr His Ile Arg Asn Glu Gln Val Arg Gln
    210   215   220

Arg Ala Lys Glu Cys Ser Gln Ala Leu Ser Leu Ile Leu Asp Ile Asp
225   230   235   240

His Gly Lys Pro Val Lys Asn Ala Leu Asp Leu Lys Phe Asp Met Glu
            245   250   255

Gln Leu Lys Asp Ser Ile Asp Arg Glu Lys Ile Ala Val Ile Gly His
        260   265   270

Ser Phe Gly Gly Ala Thr Val Ile Gln Thr Leu Ser Glu Asp Gln Arg
    275   280   285

Phe Arg Cys Gly Ile Ala Leu Asp Ala Trp Met Phe Pro Leu Gly Asp
    290   295   300

Glu Val Tyr Ser Arg Ile Pro Gln Pro Leu Phe Phe Ile Asn Ser Glu
305   310   315   320

Tyr Phe Gln Tyr Pro Ala Asn Ile Ile Lys Met Lys Lys Cys Tyr Ser
            325   330   335

Pro Asp Lys Glu Arg Lys Met Ile Thr Ile Arg Gly Ser Val His Gln
        340   345   350

Asn Phe Ala Asp Phe Thr Phe Ala Thr Gly Lys Ile Ile Gly His Met
    355   360   365

Leu Lys Leu Lys Gly Asp Ile Asp Ser Asn Val Ala Ile Asp Leu Ser
    370   375   380

Asn Lys Ala Ser Leu Ala Phe Leu Gln Lys His Leu Gly Leu His Lys
385   390   395   400

Asp Phe Asp Gln Trp Asp Cys Leu Ile Glu Gly Asp Asp Glu Asn Leu
            405   410   415

Ile Pro Gly Thr Asn Ile Asn Thr Thr Asn Gln His Ile Met Leu Gln
            420   425   430

Asn Ser Ser Gly Ile Glu Lys Tyr Asn
        435   440

<210> 2948
<211> 1044
<212> PRT
<213> Homo sapiens

<400> 2948

Met Pro Pro Gly Val Asp Cys Pro Met Glu Phe Trp Thr Lys Glu Glu
1   5   10   15

Asn Gln Ser Val Val Val Asp Phe Leu Leu Pro Thr Gly Val Tyr Leu
            20   25   30

Asn Phe Pro Val Ser Arg Asn Ala Asn Leu Ser Thr Ile Lys Gln Leu
        35   40   45

Leu Trp His Arg Ala Gln Tyr Glu Pro Leu Phe His Met Leu Ser Gly
    50   55   60

Pro Glu Ala Tyr Val Phe Thr Cys Ile Asn Gln Thr Ala Glu Gln Gln
65   70   75   80

Glu Leu Glu Asp Glu Gln Arg Arg Leu Cys Asp Val Gln Pro Phe Leu
            85   90   95

Pro Val Leu Arg Leu Val Ala Arg Glu Gly Asp Arg Val Lys Lys Leu
            100   105   110

Ile Asn Ser Gln Ile Ser Leu Leu Ile Gly Lys Gly Leu His Glu Phe
        115   120   125

Asp Ser Leu Cys Asp Pro Glu Val Asn Asp Phe Arg Ala Lys Met Cys
    130   135   140

1316

Gln Phe Cys Glu Glu Ala Ala Ala Arg Arg Gln Gln Leu Gly Trp Glu
145   150   155   160

Ala Trp Leu Gln Tyr Ser Phe Pro Leu Gln Leu Glu Pro Ser Ala Gln
            165   170   175

Thr Trp Gly Pro Gly Thr Leu Arg Leu Pro Asn Arg Ala Leu Leu Val
            180   185   190

Asn Val Lys Phe Glu Gly Ser Glu Glu Ser Phe Thr Phe Gln Val Ser
            195   200   205

Thr Lys Asp Val Pro Leu Ala Leu Met Ala Cys Ala Leu Arg Lys Lys
            210   215   220

Ala Thr Val Phe Arg Gln Pro Leu Val Glu Gln Pro Glu Asp Tyr Thr
225   230   235   240

Leu Gln Val Asn Gly Arg His Glu Tyr Leu Tyr Gly Asn Tyr Pro Leu
            245   250   255

Cys Gln Phe Gln Tyr Ile Cys Ser Cys Leu His Ser Gly Leu Thr Pro
            260   265   270

His Leu Thr Met Val His Ser Ser Ile Leu Ala Met Arg Asp Glu
            275   280   285

Gln Ser Asn Pro Ala Pro Gln Val Gln Lys Pro Arg Ala Lys Pro Pro
290   295   300

Pro Ile Pro Ala Lys Lys Pro Ser Ser Val Ser Leu Trp Ser Leu Glu
305   310   315   320

Gln Pro Phe Arg Ile Glu Leu Ile Gln Gly Ser Lys Val Asn Ala Asp
            325   330   335

Glu Arg Met Lys Leu Val Val Gln Ala Gly Leu Phe His Gly Asn Glu
            340   345   350

Met Leu Cys Lys Thr Val Ser Ser Ser Glu Val Ser Val Cys Ser Glu
            355   360   365

Pro Val Trp Lys Gln Arg Leu Glu Phe Asp Ile Asn Ile Cys Asp Leu
            370   375   380

1317

Pro Arg Met Ala Arg Leu Cys Phe Ala Leu Tyr Ala Val Ile Glu Lys
385   390   395   400

Ala Lys Lys Ala Arg Ser Thr Lys Lys Lys Ser Lys Lys Ala Asp Cys
          405   410   415

Pro Ile Ala Trp Ala Asn Leu Met Leu Phe Asp Tyr Lys Asp Gln Leu
          420   425   430

Lys Thr Gly Glu Arg Cys Leu Tyr Met Trp Pro Ser Val Pro Asp Glu
          435   440   445

Lys Gly Glu Leu Leu Asn Pro Thr Gly Thr Val Arg Ser Asn Pro Asn
     450   455   460

Thr Asp Ser Ala Ala Ala Leu Leu Ile Cys Leu Pro Glu Val Ala Pro
465   470   475   480

His Pro Val Tyr Tyr Pro Ala Leu Glu Lys Ile Leu Glu Leu Gly Arg
          485   490   495

His Ser Glu Cys Val His Val Thr Glu Glu Glu Gln Leu Gln Leu Arg
          500   505   510

Glu Ile Leu Glu Arg Arg Gly Ser Gly Glu Leu Tyr Glu His Glu Lys
          515   520   525

Asp Leu Val Trp Lys Leu Arg His Glu Val Gln Glu His Phe Pro Glu
     530   535   540

Ala Leu Ala Arg Leu Leu Leu Val Thr Lys Trp Asn Lys His Glu Asp
545   550   555   560

Val Ala Gln Met Leu Tyr Leu Leu Cys Ser Trp Pro Glu Leu Pro Val
          565   570   575

Leu Ser Ala Leu Glu Leu Leu Asp Phe Ser Phe Pro Asp Cys His Val
          580   585   590

Gly Ser Phe Ala Ile Lys Ser Leu Arg Lys Leu Thr Asp Asp Glu Leu
          595   600   605

Phe Gln Tyr Leu Leu Gln Leu Val Gln Val Leu Lys Tyr Glu Ser Tyr
     610   615   620

Leu Asp Cys Glu Leu Thr Lys Phe Leu Leu Asp Arg Ala Leu Ala Asn
625   630   635   640

Arg Lys Ile Gly His Phe Leu Phe Trp His Leu Arg Ser Glu Met His
            645   650   655

Val Pro Ser Val Ala Leu Arg Phe Gly Leu Ile Leu Glu Ala Tyr Cys
        660   665   670
                                        ı

Arg Gly Ser Thr His His Met Lys Val Leu Met Lys Gln Gly Glu Ala
        675   680   685

Leu Ser Lys Leu Lys Ala Leu Asn Asp Phe Val Lys Leu Ser Ser Gln
    690   695   700

Lys Thr Pro Lys Pro Gln Thr Lys Glu Leu Met His Leu Cys Met Arg
705   710   715   720

Gln Glu Ala Tyr Leu Glu Ala Leu Ser His Leu Gln Ser Pro Leu Asp
            725   730   735

Pro Ser Thr Leu Leu Ala Glu Val Cys Val Glu Gln Cys Thr Phe Met
        740   745   750

Asp Ser Lys Met Lys Pro Leu Trp Ile Met Tyr Ser Asn Glu Glu Ala
        755   760   765

Gly Ser Gly Gly Ser Val Gly Ile Ile Phe Lys Asn Gly Asp Asp Leu
        770   775   780

Arg Gln Asp Met Leu Thr Leu Gln Met Ile Gln Leu Met Asp Val Leu
785   790   795   800

Trp Lys Gln Glu Gly Leu Asp Leu Arg Met Thr Pro Tyr Gly Cys Leu
            805   810   815

Pro Thr Gly Asp Arg Thr Gly Leu Ile Glu Val Val Leu Arg Ser Asp
        820   825   830

Thr Ile Ala Asn Ile Gln Leu Asn Lys Ser Asn Met Ala Ala Thr Ala
    835   840   845

Ala Phe Asn Lys Asp Ala Leu Leu Asn Trp Leu Lys Ser Lys Asn Pro
850   855   860

Gly Glu Ala Leu Asp Arg Ala Ile Glu Glu Phe Thr Leu Ser Cys Ala

865   870   875   880

Gly Tyr Cys Val Ala Thr Tyr Val Leu Gly Ile Gly Asp Arg His Ser
            885   890   895

Asp Asn Ile Met Ile Arg Glu Ser Gly Gln Leu Phe His Ile Asp Phe
            900   905   910

Gly His Phe Leu Gly Asn Phe Lys Thr Lys Phe Gly Ile Asn Arg Glu
            915   920   925

Arg Val Pro Phe Ile Leu Thr Tyr Asp Phe Val His Val Ile Gln Gln
    930   935   940

Gly Lys Thr Asn Asn Ser Glu Lys Phe Glu Arg Phe Arg Gly Tyr Cys
945   950   955   960

Glu Arg Ala Tyr Thr Ile Leu Arg Arg His Gly Leu Leu Phe Leu His
            965   970   975

Leu Phe Ala Leu Met Arg Ala Ala Gly Leu Pro Glu Leu Ser Cys Ser
            980   985   990

Lys Asp Ile Gln Tyr Leu Lys Asp Ser Leu Ala Leu Gly Lys Thr Glu
            995   1000   1005

Glu Glu Ala Leu Lys His Phe Arg Val Lys Phe Asn Glu Ala Leu
    1010   1015   1020

Arg Glu Ser Trp Lys Thr Lys Val Asn Trp Leu Ala His Asn Val
    1025   1030   1035

Ser Lys Asp Asn Arg Gln
    1040

<210> 2949
<211> 167
<212> PRT
<213> Homo sapiens

<400> 2949

Met Glu His Ile His Asp Ser Asp Gly Ser Ser Ser Ser Ser His Gln
1   5   10   15

Ser Leu Lys Ser Thr Ala Lys Trp Ala Ala Ser Leu Glu Asn Leu Leu
            20   25   30

```
Glu Asp Pro Glu Gly Val Lys Arg Phe Arg Glu Phe Leu Lys Lys Glu
         35              40              45

Phe Ser Glu Glu Asn Val Leu Phe Trp Leu Ala Cys Glu Asp Phe Lys
         50              55              60

Lys Met Gln Asp Lys Thr Gln Met Gln Glu Lys Ala Lys Glu Ile Tyr
65              70              75              80

Met Thr Phe Leu Ser Ser Lys Ala Ser Ser Gln Val Asn Val Glu Gly
              85              90              95

Gln Ser Arg Leu Asn Glu Lys Ile Leu Glu Glu Pro His Pro Leu Met
         100             105             110

Phe Gln Lys Leu Gln Asp Gln Ile Phe Asn Leu Met Lys Tyr Asp Ser
         115             120             125

Tyr Ser Arg Phe Leu Lys Ser Asp Leu Phe Leu Lys His Lys Arg Thr
    130             135             140

Glu Glu Glu Glu Glu Asp Leu Pro Asp Ala Gln Thr Ala Ala Lys Arg
145             150             155             160

Ala Ser Arg Ile Tyr Asn Thr
              165
```

```
<210>  2950
<211>  263
<212>  PRT
<213>  Homo sapiens

<400>  2950

Met Val Lys Ile Ala Phe Asn Thr Pro Thr Ala Val Gln Lys Glu Glu
1               5               10              15

Ala Arg Gln Asp Val Glu Ala Leu Leu Ser Arg Thr Val Arg Thr Gln
         20              25              30

Ile Leu Thr Gly Lys Glu Leu Arg Val Ala Thr Gln Glu Lys Glu Gly
         35              40              45

Ser Ser Gly Arg Cys Met Leu Thr Leu Leu Gly Leu Ser Phe Ile Leu
         50              55              60

Ala Gly Leu Ile Val Gly Gly Ala Cys Ile Tyr Lys Tyr Phe Met Pro
```

65   70   75   80

Lys Ser Thr Ile Tyr Arg Gly Glu Met Cys Phe Phe Asp Ser Glu Asp
                85   90   95

Pro Ala Asn Ser Leu Arg Gly Gly Glu Pro Asn Phe Leu Pro Val Thr
            100   105   110

Glu Glu Ala Asp Ile Arg Glu Asp Asp Asn Ile Ala Ile Ile Asp Val
            115   120   125

Pro Val Pro Ser Phe Ser Asp Ser Asp Pro Ala Ala Ile Ile His Asp
        130   135   140

Phe Glu Lys Gly Met Thr Ala Tyr Leu Asp Leu Leu Leu Gly Asn Cys
145   150   155   160

Tyr Leu Met Pro Leu Asn Thr Ser Ile Val Met Pro Pro Lys Asn Leu
                165   170   175

Val Glu Leu Phe Gly Lys Leu Ala Ser Gly Arg Tyr Leu Pro Gln Thr
            180   185   190

Tyr Val Val Arg Glu Asp Leu Val Ala Val Glu Glu Ile Arg Asp Val
        195   200   205

Ser Asn Leu Gly Ile Phe Ile Tyr Gln Leu Cys Asn Asn Arg Lys Ser
    210   215   220

Phe Arg Leu Arg Arg Arg Asp Leu Leu Leu Gly Phe Asn Lys Arg Ala
225   230   235   240

Ile Asp Lys Cys Trp Lys Ile Arg His Phe Pro Asn Glu Phe Ile Val
            245   250   255

Glu Thr Lys Ile Cys Gln Glu
            260

<210> 2951
<211> 201
<212> PRT
<213> Homo sapiens

<400> 2951

Met Asp Pro Gly Trp Pro Cys Cys Pro Leu Pro Val Ala Phe Leu Ser
1   5   10   15

Arg Trp Leu Gln Ser Phe Val Asp Gly Leu Phe Cys Thr Gly Gly Leu
        20   25   30

Leu Arg Gln Arg Thr Cys Lys Phe Ala Gly Ala Ala Ser Gln Ala Pro
        35   40   45

His Ala Pro Ala Phe Leu Arg Ala Arg Gly Glu Pro Gln Asp Pro Leu
    50   55   60

Ser His Pro Arg Val Pro Ala Val Ser Ala Asn Cys Arg Met Trp Lys
65   70   75   80

His Leu Pro Val His Ser Ser Pro Thr Pro Arg Leu Thr Pro Leu Trp
            85   90   95

Lys Leu Gln Ala Arg Trp Leu Leu Pro Gln Leu Val Tyr Leu Gln Gly
        100   105   110

Trp Gly Ser Tyr Ser Leu Leu Arg Pro Ala Ala Leu Ile Ser Met Val
        115   120   125

Leu Leu Ala Arg Glu Phe Leu Tyr Pro Ala Lys Met Ser Val Ser Glu
    130   135   140

Val Cys Ser Ser Gly Leu Ser Ser Pro Leu Leu Glu Gln His Lys Thr
145   150   155   160

Asn Leu Ile Phe Tyr Ala Ser Gly Asp Ile Cys Ser Ala Asn Gly Lys
            165   170   175

Ser Gly Phe Asn Gln Pro Leu Pro Phe Leu Lys Thr Phe Cys Ser Thr
            180   185   190

His Arg Ile Leu Ser Cys Thr Tyr Leu
        195   200

<210>   2952
<211>   492
<212>   PRT
<213>   Homo sapiens

<400>   2952

Met Ser Asp Tyr Glu Asn Asp Asp Glu Cys Trp Ser Val Leu Glu Gly
1   5   10   15

Phe Arg Val Thr Leu Thr Ser Val Ile Asp Pro Ser Arg Ile Thr Pro

```
                    20                          25                          30


Tyr Leu Arg Gln Cys Lys Val Leu Asn Pro Asp Asp Glu Glu Gln Val
        35                  40                  45


Leu Ser Asp Pro Asn Leu Val Ile Arg Lys Arg Lys Val Gly Val Leu
    50                  55                  60


Leu Asp Ile Leu Gln Arg Thr Gly His Lys Gly Tyr Val Ala Phe Leu
65                  70                  75                  80


Glu Ser Leu Glu Leu Tyr Tyr Pro Gln Leu Tyr Lys Lys Val Thr Gly
                85                  90                  95


Lys Glu Pro Ala Arg Val Phe Ser Met Ile Ile Asp Ala Ser Gly Glu
            100                 105                 110


Ser Gly Leu Thr Gln Leu Leu Met Thr Glu Val Met Lys Leu Gln Lys
        115                 120                 125


Lys Val Gln Asp Leu Thr Ala Leu Leu Ser Ser Lys Asp Asp Phe Ile
    130                 135                 140


Lys Glu Leu Arg Val Lys Asp Ser Leu Leu Arg Lys His Gln Glu Arg
145                 150                 155                 160


Val Gln Arg Leu Lys Glu Glu Cys Glu Ala Gly Ser Arg Glu Leu Lys
            165                 170                 175


Arg Cys Lys Glu Glu Asn Tyr Asp Leu Ala Met Arg Leu Ala His Gln
            180                 185                 190


Ser Glu Glu Lys Gly Ala Ala Leu Met Arg Asn Arg Asp Leu Gln Leu
        195                 200                 205


Glu Ile Asp Gln Leu Lys His Ser Leu Met Lys Ala Glu Asp Asp Cys
    210                 215                 220


Lys Val Glu Arg Lys His Thr Leu Lys Leu Arg His Ala Met Glu Gln
225                 230                 235                 240


Arg Pro Ser Gln Glu Leu Leu Trp Glu Leu Gln Gln Glu Lys Ala Leu
            245                 250                 255


Leu Gln Ala Arg Val Gln Glu Leu Glu Ala Ser Val Gln Glu Gly Lys
        260                 265                 270
```

                                      1324

```
Leu Asp Arg Ser Ser Pro Tyr Ile Gln Val Leu Glu Glu Asp Trp Arg
    275             280             285

Gln Ala Leu Arg Asp His Gln Glu Gln Ala Asn Thr Ile Phe Ser Leu
    290             295             300

Arg Lys Asp Leu Arg Gln Gly Glu Ala Arg Arg Leu Arg Cys Met Glu
305             310             315             320

Glu Lys Glu Met Phe Glu Leu Gln Cys Leu Ala Leu Arg Lys Asp Ser
            325             330             335

Lys Met Tyr Lys Asp Arg Ile Glu Ala Ile Leu Leu Gln Met Glu Glu
        340             345             350

Val Ala Ile Glu Arg Asp Gln Ala Ile Ala Thr Arg Glu Glu Leu His
        355             360             365

Ala Gln His Ala Arg Gly Leu Gln Glu Lys Asp Ala Leu Arg Lys Gln
    370             375             380

Val Arg Glu Leu Gly Glu Lys Ala Asp Glu Leu Gln Leu Gln Val Phe
385             390             395             400

Gln Cys Glu Ala Gln Leu Leu Ala Val Glu Gly Arg Leu Arg Arg Gln
            405             410             415

Gln Leu Glu Thr Leu Val Leu Ser Ser Asp Leu Glu Asp Gly Ser Pro
            420             425             430

Arg Arg Ser Gln Glu Leu Ser Leu Pro Gln Asp Leu Glu Asp Thr Gln
    435             440             445

Leu Ser Asp Lys Gly Cys Leu Ala Gly Gly Gly Ser Pro Lys Gln Pro
    450             455             460

Phe Ala Ala Leu His Gln Glu Gln Val Leu Arg Asn Pro His Asp Ala
465             470             475             480

Gly Pro Ala Gly Leu Pro Gly Ile Gly Ala Val Cys
                485             490
```

<210> 2953
<211> 92
<212> PRT

<213>   Homo sapiens

<400>   2953

```
Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala
1               5                   10                  15


Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
            20                  25                  30


Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
            35                  40                  45


Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
            50                  55                  60


Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65                  70                  75                  80


Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
                85                  90
```

<210>   2954
<211>   266
<212>   PRT
<213>   Homo sapiens

<400>   2954

```
Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Thr Ala Leu Thr
1               5                   10                  15


Val Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
            20                  25                  30


Arg Pro Arg Phe Leu Trp Gln Leu Lys Phe Glu Cys His Phe Phe Asn
            35                  40                  45


Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Cys Ile Tyr Asn Gln Glu
            50                  55                  60


Glu Ser Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65                  70                  75                  80


Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu
                85                  90                  95


Leu Glu Gln Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
                100                 105                 110
```

```
Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Glu Pro Lys Val
        115                 120                 125

Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
        130                 135                 140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145                 150                 155                 160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
                165                 170                 175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
                180                 185                 190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
        195                 200                 205

Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
        210                 215                 220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225                 230                 235                 240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
                245                 250                 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
                260                 265
```

```
<210>  2955
<211>  359
<212>  PRT
<213>  Homo sapiens

<400>  2955

Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala Pro
1               5                   10                  15

Leu Lys Lys Ser Ile Ser Ser Arg Leu Gly Gln Asp Pro Gly Ala Asp
                20                  25                  30

Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro Ala Val Leu
        35                  40                  45
```

```
Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly Asp Lys Ala Ala
    50              55              60


Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg Ala Val Thr Ser Pro
65              70              75              80


Ala Val Gly Arg Ile Leu Pro Cys Arg Thr Thr Cys Leu Arg Tyr Leu
            85              90              95


Leu Leu Gly Leu Leu Leu Thr Cys Leu Leu Leu Gly Val Thr Ala Ile
        100             105             110


Cys Leu Gly Val Arg Tyr Leu Gln Val Ser Gln Gln Leu Gln Gln Thr
    115             120             125


Asn Arg Val Leu Glu Val Thr Asn Ser Ser Leu Arg Gln Gln Leu Arg
    130             135             140


Leu Lys Ile Thr Gln Leu Gly Gln Ser Ala Glu Asp Leu Gln Gly Ser
145             150             155             160


Arg Arg Glu Leu Ala Gln Ser Gln Glu Ala Leu Gln Val Glu Gln Arg
            165             170             175


Ala His Gln Ala Ala Glu Gly Gln Leu Gln Ala Cys Gln Ala Asp Arg
        180             185             190


Gln Lys Thr Lys Glu Thr Leu Gln Ser Glu Glu Gln Gln Arg Arg Ala
    195             200             205


Leu Glu Gln Lys Leu Ser Asn Met Glu Asn Arg Leu Lys Pro Phe Phe
    210             215             220


Thr Cys Gly Ser Ala Asp Thr Cys Cys Pro Ser Gly Trp Ile Met His
225             230             235             240


Gln Lys Ser Cys Phe Tyr Ile Ser Leu Thr Ser Lys Asn Trp Gln Glu
            245             250             255


Ser Gln Lys Gln Cys Glu Thr Leu Ser Ser Lys Leu Ala Thr Phe Ser
        260             265             270


Glu Ile Tyr Pro Gln Ser His Ser Tyr Tyr Phe Leu Asn Ser Leu Leu
        275             280             285


Pro Asn Gly Gly Ser Gly Asn Ser Tyr Trp Thr Gly Leu Ser Ser Asn
```

1328

```
     290                    295                 300
```

Lys Asp Trp Lys Leu Thr Asp Asp Thr Gln Arg Thr Arg Thr Tyr Ala
305   310   315   320

Gln Ser Ser Lys Cys Asn Lys Val His Lys Thr Trp Ser Trp Trp Thr
                325   330   335

Leu Glu Ser Glu Ser Cys Arg Ser Ser Leu Pro Tyr Ile Cys Glu Met
                340   345   350

Thr Ala Phe Arg Phe Pro Asp
            355

```
<210>  2956
<211>  643
<212>  PRT
<213>  Homo sapiens

<400>  2956
```

Met Gln Ala Pro Arg Glu Leu Ala Val Gly Ile Asp Leu Gly Thr Thr
1   5   10   15

Tyr Ser Cys Val Gly Val Phe Gln Gln Gly Arg Val Glu Ile Leu Ala
                20   25   30

Asn Asp Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp
            35   40   45

Thr Glu Arg Leu Val Gly Asp Ala Ala Lys Ser Gln Ala Ala Leu Asn
        50   55   60

Pro His Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe
65   70   75   80

Ala Asp Thr Thr Val Gln Ser Asp Met Lys His Trp Pro Phe Arg Val
                85   90   95

Val Ser Glu Gly Gly Lys Pro Lys Val Pro Val Ser Tyr Arg Gly Glu
                100   105   110

Asp Lys Thr Phe Tyr Pro Glu Glu Ile Ser Ser Met Val Leu Ser Lys
        115   120   125

Met Lys Glu Thr Ala Glu Ala Tyr Leu Gly Gln Pro Val Lys His Ala
        130   135   140

1329

Val Ile Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr
145   150   155   160

Lys Asp Ala Gly Ala Ile Ala Gly Leu Asn Val Leu Arg Ile Ile Asn
                165   170   175

Glu Pro Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Arg Arg Gly Ala
            180   185   190

Gly Glu Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp
        195   200   205

Val Ser Val Leu Ser Ile Asp Ala Gly Val Phe Glu Val Lys Ala Thr
    210   215   220

Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val
225   230   235   240

Asn His Phe Met Glu Glu Phe Arg Arg Lys His Gly Lys Asp Leu Ser
            245   250   255

Gly Asn Lys Arg Ala Leu Gly Arg Leu Arg Thr Ala Cys Glu Arg Ala
        260   265   270

Lys Arg Thr Leu Ser Ser Ser Thr Gln Ala Thr Leu Glu Ile Asp Ser
        275   280   285

Leu Phe Glu Gly Val Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe
    290   295   300

Glu Glu Leu Cys Ser Asp Leu Phe Arg Ser Thr Leu Glu Pro Val Glu
305   310   315   320

Lys Ala Leu Arg Asp Ala Lys Leu Asp Lys Ala Gln Ile His Asp Val
            325   330   335

Val Leu Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu
        340   345   350

Gln Asp Phe Phe Asn Gly Lys Glu Leu Asn Lys Ser Ile Asn Pro Asp
        355   360   365

Glu Ala Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Val Leu Met Gly
    370   375   380

1330

```
Asp Lys Cys Glu Lys Val Gln Asp Leu Leu Leu Leu Asp Val Ala Pro
385             390             395                 400

Leu Ser Leu Gly Leu Glu Thr Ala Gly Gly Val Met Thr Thr Leu Ile
                405             410                 415

Gln Arg Asn Ala Thr Ile Pro Thr Lys Gln Thr Gln Thr Phe Thr Thr
            420             425             430

Tyr Ser Asp Asn Gln Pro Gly Val Phe Ile Gln Val Tyr Glu Gly Glu
            435             440             445

Arg Ala Met Thr Lys Asp Asn Asn Leu Leu Gly Arg Phe Glu Leu Ser
    450             455             460

Gly Ile Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe
465             470             475                 480

Asp Ile Asp Ala Asn Gly Ile Leu Ser Val Thr Ala Thr Asp Arg Ser
            485             490             495

Thr Gly Lys Ala Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu
            500             505             510

Ser Lys Glu Glu Val Glu Arg Met Val His Glu Ala Glu Gln Tyr Lys
    515             520             525

Ala Glu Asp Glu Ala Gln Arg Asp Arg Val Ala Ala Lys Asn Ser Leu
    530             535             540

Glu Ala His Val Phe His Val Lys Gly Ser Leu Gln Glu Glu Ser Leu
545             550             555                 560

Arg Asp Lys Ile Pro Glu Glu Asp Arg Arg Lys Met Gln Asp Lys Cys
            565             570             575

Arg Glu Val Leu Ala Trp Leu Glu His Asn Gln Leu Ala Glu Lys Glu
            580             585             590

Glu Tyr Glu His Gln Lys Arg Glu Leu Glu Gln Ile Cys Arg Pro Ile
    595             600             605

Phe Ser Arg Leu Tyr Gly Gly Pro Gly Val Pro Gly Gly Ser Ser Cys
    610             615             620

Gly Thr Gln Ala Arg Gln Gly Asp Pro Ser Thr Gly Pro Ile Ile Glu
```

625   630   635   640

Glu Val Asp

<210>   2957
<211>   565
<212>   PRT
<213>   Homo sapiens

<400>   2957

Met Ala Glu Gly Lys Ala Gly Gly Ala Ala Gly Leu Phe Ala Lys Gln
1   5   10   15

Val Gln Lys Lys Phe Ser Arg Ala Gln Glu Lys Val Leu Gln Lys Leu
                20   25   30

Gly Lys Ala Val Glu Thr Lys Asp Glu Arg Phe Glu Gln Ser Ala Asn
        35   40   45

Asn Phe Tyr Gln Gln Gln Ala Glu Gly His Lys Leu Tyr Lys Asp Leu
        50   55   60

Lys Asn Phe Leu Ser Ala Val Lys Val Met His Glu Ser Ser Lys Arg
65   70   75   80

Val Ser Glu Thr Leu Gln Glu Ile Tyr Ser Ser Glu Trp Asp Gly His
                85   90   95

Glu Glu Leu Lys Ala Ile Val Trp Asn Asn Asp Leu Leu Trp Glu Asp
                100   105   110

Tyr Glu Glu Lys Leu Ala Asp Gln Ala Val Arg Thr Met Glu Ile Tyr
        115   120   125

Val Ala Gln Phe Ser Glu Ile Lys Glu Arg Ile Ala Lys Arg Gly Arg
        130   135   140

Lys Leu Val Asp Tyr Asp Ser Ala Arg His His Leu Glu Ala Val Gln
145   150   155   160

Asn Ala Lys Lys Lys Asp Glu Ala Lys Thr Ala Lys Ala Glu Glu Glu
                165   170   175

Phe Asn Lys Ala Gln Thr Val Phe Glu Asp Leu Asn Gln Glu Leu Leu
        180   185   190

1332

Glu Glu Leu Pro Ile Leu Tyr Asn Ser Arg Ile Gly Cys Tyr Val Thr
        195   200   205

Ile Phe Gln Asn Ile Ser Asn Leu Arg Asp Val Phe Tyr Arg Glu Met
    210   215   220

Ser Lys Leu Asn His Asn Leu Tyr Glu Val Met Ser Lys Leu Glu Lys
225   230   235   240

Gln His Ser Asn Lys Val Phe Val Val Lys Gly Leu Ser Ser Ser Ser
            245   250   255

Arg Arg Ser Leu Val Ile Ser Pro Pro Val Arg Thr Ala Thr Val Ser
        260   265   270

Ser Pro Leu Thr Ser Pro Thr Ser Pro Ser Thr Leu Ser Leu Lys Ser
        275   280   285

Glu Ser Glu Ser Val Ser Ala Thr Glu Asp Leu Ala Pro Asp Ala Ala
    290   295   300

Gln Gly Glu Asp Asn Ser Glu Ile Lys Glu Leu Leu Glu Glu Glu Glu
305   310   315   320

Ile Glu Lys Glu Gly Ser Glu Ala Ser Ser Ser Glu Glu Asp Glu Pro
            325   330   335

Leu Pro Ala Cys Asn Gly Pro Ala Gln Ala Gln Pro Ser Pro Thr Thr
        340   345   350

Glu Arg Ala Lys Ser Gln Glu Glu Val Leu Pro Ser Ser Thr Thr Pro
        355   360   365

Ser Pro Gly Gly Ala Leu Ser Pro Ser Gly Gln Pro Ser Ser Ser Ala
    370   375   380

Thr Glu Val Val Leu Arg Thr Arg Thr Ala Ser Glu Gly Ser Glu Gln
385   390   395   400

Pro Lys Lys Arg Ala Ser Ile Gln Arg Thr Ser Ala Pro Pro Ser Arg
            405   410   415

Pro Pro Pro Pro Arg Ala Thr Ala Ser Pro Arg Pro Ser Ser Gly Asn
            420   425   430

```
Ile Pro Ser Ser Pro Thr Ala Ser Gly Gly Gly Ser Pro Thr Ser Pro
        435             440             445

Arg Ala Ser Leu Gly Thr Gly Thr Ala Ser Pro Arg Thr Ser Leu Glu
        450             455             460

Val Ser Pro Asn Pro Glu Pro Pro Glu Lys Pro Val Arg Thr Pro Glu
465             470             475             480

Ala Lys Glu Asn Glu Asn Ile His Asn Gln Asn Pro Glu Glu Leu Cys
                485             490             495

Thr Ser Pro Thr Leu Met Thr Ser Gln Val Ala Ser Glu Pro Gly Glu
        500             505             510

Ala Lys Lys Met Glu Asp Lys Glu Lys Asp Asn Lys Leu Ile Ser Ala
        515             520             525

Asp Ser Ser Glu Gly Gln Asp Gln Leu Gln Val Ser Met Val Pro Glu
        530             535             540

Asn Asn Asn Leu Thr Ala Pro Glu Pro Gln Glu Glu Val Ser Thr Ser
545             550             555             560

Glu Asn Pro Gln Leu
            565


<210>  2958
<211>  349
<212>  PRT
<213>  Homo sapiens

<400>  2958

Met Glu Thr Pro Pro Val Asn Thr Ile Gly Glu Lys Asp Thr Ser Gln
1           5               10              15

Pro Gln Gln Glu Trp Glu Lys Asn Leu Arg Glu Asn Leu Asp Ser Val
            20              25              30

Ile Gln Ile Arg Gln Gln Pro Arg Asp Pro Pro Thr Glu Thr Leu Glu
        35              40              45

Leu Glu Val Ser Pro Asp Pro Ala Ser Gln Ile Leu Glu His Thr Gln
        50              55              60

Gly Ala Glu Lys Leu Val Ala Glu Leu Glu Gly Asp Ser His Lys Ser
65              70              75              80
```

His Gly Ser Thr Ser Gln Met Pro Glu Ala Leu Gln Ala Ser Asp Leu
            85   90   95

Trp Tyr Cys Pro Asp Gly Ser Phe Val Lys Lys Ile Val Ile Arg Gly
            100   105   110

His Gly Leu Asp Lys Pro Lys Leu Gly Ser Cys Cys Arg Val Leu Ala
        115   120   125

Leu Gly Phe Pro Phe Gly Ser Gly Pro Pro Glu Gly Trp Thr Glu Leu
    130   135   140

Thr Met Gly Val Gly Pro Trp Arg Glu Glu Thr Trp Gly Glu Leu Ile
145   150   155   160

Glu Lys Cys Leu Glu Ser Met Cys Gln Gly Glu Glu Ala Glu Leu Gln
            165   170   175

Leu Pro Gly His Ser Gly Pro Pro Val Arg Leu Thr Leu Ala Ser Phe
            180   185   190

Thr Gln Gly Arg Asp Ser Trp Glu Leu Glu Thr Ser Glu Lys Glu Ala
        195   200   205

Leu Ala Arg Glu Glu Arg Ala Arg Gly Thr Glu Leu Phe Arg Ala Gly
    210   215   220

Asn Pro Glu Gly Ala Ala Arg Cys Tyr Gly Arg Ala Leu Arg Leu Leu
225   230   235   240

Leu Thr Leu Pro Pro Pro Gly Pro Pro Glu Arg Thr Val Leu His Ala
            245   250   255

Asn Leu Ala Ala Cys Gln Leu Leu Leu Gly Gln Pro Gln Leu Ala Ala
        260   265   270

Gln Ser Cys Asp Arg Val Leu Glu Arg Glu Pro Gly His Leu Lys Ala
        275   280   285

Leu Tyr Arg Arg Gly Val Ala Gln Ala Ala Leu Gly Asn Leu Glu Lys
    290   295   300

Ala Thr Ala Asp Leu Lys Lys Val Leu Ala Ile Asp Pro Lys Asn Arg
305   310   315   320

```
Ala Ala Gln Glu Glu Leu Gly Lys Val Val Ile Gln Gly Lys Asn Gln
            325             330             335

Asp Ala Gly Leu Ala Gln Gly Leu Arg Lys Met Phe Gly
            340             345


<210>    2959
<211>    620
<212>    PRT
<213>    Homo sapiens

<400>    2959

Met Asn Asn Phe Ile Leu Leu Glu Glu Gln Leu Ile Lys Lys Ser Gln
1               5               10              15

Gln Lys Arg Arg Thr Ser Pro Ser Asn Phe Lys Val Arg Phe Phe Val
            20              25              30

Leu Thr Lys Ala Ser Leu Ala Tyr Phe Glu Asp Arg His Gly Lys Lys
        35              40              45

Arg Thr Leu Lys Gly Ser Ile Glu Leu Ser Arg Ile Lys Cys Val Glu
        50              55              60

Ile Val Lys Ser Asp Ile Ser Ile Pro Cys His Tyr Lys Tyr Pro Phe
65              70              75              80

Gln Val Val His Asp Asn Tyr Leu Leu Tyr Val Phe Ala Pro Asp Arg
            85              90              95

Glu Ser Arg Gln Arg Trp Val Leu Ala Leu Lys Glu Glu Thr Arg Asn
            100             105             110

Asn Asn Ser Leu Val Pro Lys Tyr His Pro Asn Phe Trp Met Asp Gly
        115             120             125

Lys Trp Arg Cys Cys Ser Gln Leu Glu Lys Leu Ala Thr Gly Cys Ala
        130             135             140

Gln Tyr Asp Pro Thr Lys Asn Ala Ser Lys Lys Pro Leu Pro Pro Thr
145             150             155             160

Pro Glu Asp Asn Arg Arg Pro Leu Trp Glu Pro Glu Glu Thr Val Val
            165             170             175

Ile Ala Leu Tyr Asp Tyr Gln Thr Asn Asp Pro Gln Glu Leu Ala Leu
```

```
              180                    185                    190


    Arg Arg Asn Glu Glu Tyr Cys Leu Leu Asp Ser Ser Glu Ile His Trp
            195                 200                 205


    Trp Arg Val Gln Asp Arg Asn Gly His Glu Gly Tyr Val Pro Ser Ser
        210                 215                 220


    Tyr Leu Val Glu Lys Ser Pro Asn Asn Leu Glu Thr Tyr Glu Trp Tyr
    225                 230                 235                 240


    Asn Lys Ser Ile Ser Arg Asp Lys Ala Glu Lys Leu Leu Leu Asp Thr
                    245                 250                 255


    Gly Lys Glu Gly Ala Phe Met Val Arg Asp Ser Arg Thr Ala Gly Thr
                260                 265                 270


    Tyr Thr Val Ser Val Phe Thr Lys Ala Val Val Ser Glu Asn Asn Pro
                275                 280                 285


    Cys Ile Lys His Tyr His Ile Lys Glu Thr Asn Asp Asn Pro Lys Arg
        290                 295                 300


    Tyr Tyr Val Ala Glu Lys Tyr Val Phe Asp Ser Ile Pro Leu Leu Ile
    305                 310                 315                 320


    Asn Tyr His Gln His Asn Gly Gly Gly Leu Val Thr Arg Leu Arg Tyr
                    325                 330                 335


    Pro Val Cys Phe Gly Arg Gln Lys Ala Pro Val Thr Ala Gly Leu Arg
                340                 345                 350


    Tyr Gly Lys Trp Val Ile Asp Pro Ser Glu Leu Thr Phe Val Gln Glu
            355                 360                 365


    Ile Gly Ser Gly Gln Phe Gly Leu Val His Leu Gly Tyr Trp Leu Asn
        370                 375                 380


    Lys Asp Lys Val Ala Ile Lys Thr Ile Arg Glu Gly Ala Met Ser Glu
    385                 390                 395                 400


    Glu Asp Phe Ile Glu Glu Ala Glu Val Met Met Lys Leu Ser His Pro
                    405                 410                 415


    Lys Leu Val Gln Leu Tyr Gly Val Cys Leu Glu Gln Ala Pro Ile Cys
                420                 425                 430
```

```
Leu Val Phe Glu Phe Met Glu His Gly Cys Leu Ser Asp Tyr Leu Arg
        435                 440                 445


Thr Gln Arg Gly Leu Phe Ala Ala Glu Thr Leu Leu Gly Met Cys Leu
        450                 455                 460


Asp Val Cys Glu Gly Met Ala Tyr Leu Glu Glu Ala Cys Val Ile His
465                 470                 475                 480


Arg Asp Leu Ala Ala Arg Asn Cys Leu Val Gly Glu Asn Gln Val Ile
                485                 490                 495


Lys Val Ser Asp Phe Gly Met Thr Arg Phe Val Leu Asp Asp Gln Tyr
                500                 505                 510


Thr Ser Ser Thr Gly Thr Lys Phe Pro Val Lys Trp Ala Ser Pro Glu
        515                 520                 525


Val Phe Ser Phe Ser Arg Tyr Ser Ser Lys Ser Asp Val Trp Ser Phe
        530                 535                 540


Gly Val Leu Met Trp Glu Val Phe Ser Glu Gly Lys Ile Pro Tyr Glu
545                 550                 555                 560


Asn Arg Ser Asn Ser Glu Val Val Glu Asp Ile Ser Thr Gly Phe Arg
                565                 570                 575


Leu Tyr Lys Pro Arg Leu Ala Ser Thr His Val Tyr Gln Ile Met Asn
                580                 585                 590


His Cys Trp Lys Glu Arg Pro Glu Asp Arg Pro Ala Phe Ser Arg Leu
        595                 600                 605


Leu Arg Gln Leu Ala Glu Ile Ala Glu Ser Gly Leu
        610                 615                 620


<210>   2960
<211>   262
<212>   PRT
<213>   Homo sapiens

<400>   2960

Met Asp Pro Arg Leu Ser Thr Val Arg Gln Thr Cys Cys Cys Phe Asn
1               5                   10                  15
```

Val Arg Ile Ala Thr Thr Ala Leu Ala Ile Tyr His Val Ile Met Ser
         20   25   30

Val Leu Leu Phe Ile Glu His Ser Val Glu Val Ala His Gly Lys Ala
         35   40   45

Ser Cys Lys Leu Ser Gln Met Gly Tyr Leu Arg Ile Ala Asp Leu Ile
    50   55   60

Ser Ser Phe Leu Leu Ile Thr Met Leu Phe Ile Ile Ser Leu Ser Leu
65   70   75   80

Leu Ile Gly Val Val Lys Asn Arg Glu Lys Tyr Leu Leu Pro Phe Leu
             85   90   95

Ser Leu Gln Ile Met Asp Tyr Leu Leu Cys Leu Leu Thr Leu Leu Gly
             100   105   110

Ser Tyr Ile Glu Leu Pro Ala Tyr Leu Lys Leu Ala Ser Arg Ser Arg
         115   120   125

Ala Ser Ser Ser Lys Phe Pro Leu Met Thr Leu Gln Leu Leu Asp Phe
    130   135   140

Cys Leu Ser Ile Leu Thr Leu Cys Ser Ser Tyr Met Glu Val Pro Thr
145   150   155   160

Tyr Leu Asn Phe Lys Ser Met Asn His Met Asn Tyr Leu Pro Ser Gln
             165   170   175

Glu Asp Met Pro His Asn Gln Phe Ile Lys Met Met Ile Ile Phe Ser
         180   185   190

Ile Ala Phe Ile Thr Val Leu Ile Phe Lys Val Tyr Met Phe Lys Cys
         195   200   205

Val Trp Arg Cys Tyr Arg Leu Ile Lys Cys Met Asn Ser Val Glu Glu
    210   215   220

Lys Arg Asn Ser Lys Met Leu Gln Lys Val Val Leu Pro Ser Tyr Glu
225   230   235   240

Glu Ala Leu Ser Leu Pro Ser Lys Thr Pro Glu Gly Gly Pro Ala Pro
             245   250   255

Pro Pro Tyr Ser Glu Val

```
<210>  2961
<211>  467
<212>  PRT
<213>  Homo sapiens

<400>  2961
```

Met Gln Met Asp Asn Arg Leu Pro Pro Lys Lys Val Pro Gly Phe Cys
1   5   10   15

Ser Phe Arg Tyr Gly Leu Ser Phe Leu Val His Cys Cys Asn Val Ile
            20   25   30

Ile Thr Ala Gln Arg Ala Cys Leu Asn Leu Thr Met Val Val Met Val
        35   40   45

Asn Ser Thr Asp Pro His Gly Leu Pro Asn Thr Ser Thr Lys Lys Leu
    50   55   60

Leu Asp Asn Ile Lys Asn Pro Met Tyr Asn Trp Ser Pro Asp Ile Gln
65   70   75   80

Gly Ile Ile Leu Ser Ser Thr Ser Tyr Gly Val Ile Ile Ile Gln Val
                85   90   95

Pro Val Gly Tyr Phe Ser Gly Ile Tyr Ser Thr Lys Lys Met Ile Gly
            100   105   110

Phe Ala Leu Cys Leu Ser Ser Val Leu Ser Leu Leu Ile Pro Pro Ala
            115   120   125

Ala Gly Ile Gly Val Ala Trp Val Val Val Cys Arg Ala Val Gln Gly
    130   135   140

Ala Ala Gln Gly Ile Val Ala Thr Ala Gln Phe Glu Ile Tyr Val Lys
145   150   155   160

Trp Ala Pro Pro Leu Glu Arg Gly Arg Leu Thr Ser Met Ser Thr Ser
                165   170   175

Gly Phe Leu Leu Gly Pro Phe Ile Val Leu Leu Val Thr Gly Val Ile
            180   185   190

Cys Glu Ser Leu Gly Trp Pro Met Val Phe Tyr Ile Phe Gly Ala Cys
            195   200   205

Gly Cys Ala Val Cys Leu Leu Trp Phe Val Leu Phe Tyr Asp Asp Pro
210   215   220

Lys Asp His Pro Cys Ile Ser Ile Ser Glu Lys Glu Tyr Ile Thr Ser
225   230   235   240

Ser Leu Val Gln Gln Val Ser Ser Ser Arg Gln Ser Leu Pro Ile Lys
245   250   255

Ala Ile Leu Lys Ser Leu Pro Val Trp Ala Ile Ser Ile Gly Ser Phe
260   265   270

Thr Phe Phe Trp Ser His Asn Ile Met Thr Leu Tyr Thr Pro Met Phe
275   280   285

Ile Asn Ser Met Leu His Val Asn Ile Lys Glu Asn Gly Phe Leu Ser
290   295   300

Ser Leu Pro Tyr Leu Phe Ala Trp Ile Cys Gly Asn Leu Ala Gly Gln
305   310   315   320

Leu Ser Asp Phe Phe Leu Thr Arg Asn Ile Leu Ser Val Ile Ala Val
325   330   335

Arg Lys Leu Phe Thr Ala Ala Gly Phe Leu Leu Pro Ala Ile Phe Gly
340   345   350

Val Cys Leu Pro Tyr Leu Ser Ser Thr Phe Tyr Ser Ile Val Ile Phe
355   360   365

Leu Ile Leu Ala Gly Ala Thr Gly Ser Phe Cys Leu Gly Gly Val Phe
370   375   380

Ile Asn Gly Leu Asp Ile Ala Pro Arg Tyr Phe Gly Phe Ile Lys Ala
385   390   395   400

Cys Ser Thr Leu Thr Gly Met Ile Gly Gly Leu Ile Ala Ser Thr Leu
405   410   415

Thr Gly Leu Ile Leu Lys Gln Asp Pro Glu Ser Ala Trp Phe Lys Thr
420   425   430

Phe Ile Leu Met Ala Ala Ile Asn Val Thr Gly Leu Ile Phe Tyr Leu
435   440   445

1341

Ile Val Ala Thr Ala Glu Ile Gln Asp Trp Ala Lys Glu Lys Gln His
     450   455   460

Thr Arg Leu
465

<210> 2962
<211> 444
<212> PRT
<213> Homo sapiens

<400> 2962

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln
1   5   10   15

Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val
             20   25   30

Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro
         35   40   45

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu
     50   55   60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile
65   70   75   80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly
                 85   90   95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
             100   105   110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile
         115   120   125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr
     130   135   140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala
145   150   155   160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile
                 165   170   175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val
             180   185   190

1342

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu
        195   200   205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
        210   215   220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225   230   235   240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
            245   250   255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
            260   265   270

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
        275   280   285

Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg
    290   295   300

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305   310   315   320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
            325   330   335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
            340   345   350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
        355   360   365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
    370   375   380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385   390   395   400

Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
            405   410   415

Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
        420   425   430

```
Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
        435                 440
```

```
<210>    2963
<211>    272
<212>    PRT
<213>    Homo sapiens

<400>    2963
```

```
Arg Cys Lys Pro Ile Ser Gly His Asn Ser Leu Phe Trp Tyr Arg Gln
1                5                   10                  15
```

```
Thr Met Met Arg Gly Leu Glu Leu Leu Ile Tyr Phe Asn Asn Asn Val
             20                  25                  30
```

```
Pro Ile Asp Asp Ser Gly Met Pro Glu Asp Arg Phe Ser Ala Lys Met
         35                  40                  45
```

```
Pro Asn Ala Ser Phe Ser Thr Leu Lys Ile Gln Pro Ser Glu Pro Arg
    50                  55                  60
```

```
Asp Ser Ala Val Tyr Phe Cys Ala Ser Ser Phe Ser Thr Cys Ser Ala
65                  70                  75                  80
```

```
Asn Tyr Gly Tyr Thr Phe Gly Ser Gly Thr Arg Leu Thr Val Val Glu
                85                  90                  95
```

```
Asp Leu Asn Lys Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro Ser
             100                 105                 110
```

```
Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu Ala
        115                 120                 125
```

```
Thr Gly Phe Phe Pro Asp His Val Glu Leu Ser Trp Trp Val Asn Gly
    130                 135                 140
```

```
Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys Glu
145                 150                 155                 160
```

```
Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu Ser Ser Arg Leu Arg
                165                 170                 175
```

```
Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn His Phe Arg Cys Gln
             180                 185                 190
```

```
Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp Arg
```

```
            195                  200                  205


   Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg Ala
       210                  215                  220


   Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln Gly Val Leu Ser Ala
   225                  230                  235                  240


   Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala Thr Leu Tyr Ala Val
                    245                  250                  255


   Leu Val Ser Ala Leu Val Leu Met Ala Met Val Lys Arg Lys Asp Phe
                260                  265                  270
```

```
<210>   2964
<211>   276
<212>   PRT
<213>   Homo sapiens

<400>   2964

Met Tyr Arg Ile Ser Gln Leu Met Ser Thr Pro Val Ala Ser Ser Ser
1               5                   10                  15


Arg Leu Glu Arg Glu Tyr Ala Gly Glu Leu Ser Pro Thr Cys Ile Phe
            20                  25                  30


Pro Ser Phe Thr Cys Asp Ser Leu Asp Gly Tyr His Ser Phe Glu Cys
        35                  40                  45


Gly Ser Ile Asp Pro Leu Thr Gly Ser His Tyr Thr Cys Arg Arg Ser
    50                  55                  60


Pro Arg Leu Leu Thr Asn Gly Tyr Tyr Ile Trp Thr Glu Asp Ser Phe
65                  70                  75                  80


Leu Cys Asp Lys Asp Gly Asn Ile Thr Leu Asn Pro Ser Gln Thr Ser
                85                  90                  95


Val Met Tyr Lys Glu Asn Leu Val Ser Thr Ser Lys Ser Trp Leu His
            100                 105                 110


Gly Ser Ile Phe Gly Asp Ile Asn Ser Ser Pro Ser Glu Asp Asn Trp
        115                 120                 125


Leu Lys Gly Thr Arg Arg Leu Asp Thr Asp His Cys Asn Gly Asn Ala
    130                 135                 140
```

```
Asp Asp Leu Asp Cys Ser Ser Leu Thr Asp Asp Trp Glu Ser Gly Lys
145             150             155             160

Met Asn Ala Glu Ser Val Ile Thr Ser Ser Ser Ser His Ile Ile Ser
                165             170             175

Gln Pro Pro Gly Gly Asn Ser His Ser Leu Ser Leu Gln Ser Gln Leu
            180             185             190

Thr Ala Ser Glu Arg Phe Gln Glu Asn Ser Ser Asp His Ser Glu Thr
            195             200             205

Arg Leu Leu Gln Glu Val Phe Phe Gln Ala Ile Leu Leu Ala Val Cys
    210             215             220

Leu Ile Thr Ser Ala Cys Ala Arg Trp Phe Met Gly Glu Ile Leu Ala
225             230             235             240

Ser Val Phe Thr Cys Ser Leu Met Ile Thr Val Ala Tyr Val Lys Ser
                245             250             255

Leu Phe Leu Ser Leu Ala Ser Tyr Phe Lys Thr Thr Ala Cys Ala Arg
            260             265             270

Phe Val Lys Ile
        275


<210>  2965
<211>  133
<212>  PRT
<213>  Homo sapiens

<400>  2965

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1               5               10              15

Gly Ala Tyr Gly Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala
            20              25              30

Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser
        35              40              45

Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln
    50              55              60

Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
```

```
             65                    70                  75                    80
```

Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
                     85   90   95

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
            100   105   110

Tyr Cys Gln Gln Tyr Asp Thr Ile Pro Thr Phe Gly Gly Gly Thr Lys
        115   120   125

Val Glu Ile Lys Arg
    130

<210> 2966
<211> 369
<212> PRT
<213> Homo sapiens

<400> 2966

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
1   5   10   15

Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly
            20   25   30

Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp
        35   40   45

Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
    50   55   60

Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65   70   75   80

Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn
                85   90   95

Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr
            100   105   110

Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe
        115   120   125

Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln
    130   135   140

Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu
145   150   155   160

Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn
                165   170   175

Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp
            180   185   190

Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe
        195   200   205

Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg
    210   215   220

Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp
225   230   235   240

Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Pro Phe
            245   250   255

Leu Phe Ala Leu Glu Ala Val Val Ile Ser Val Gly Ser Met Gly Leu
            260   265   270

Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu Arg Thr Met Pro
        275   280   285

Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val Thr Glu Tyr His
    290   295   300

Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys Gly Leu Ala Glu Ser
305   310   315   320

Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu Val Ser Glu Ile Pro
            325   330   335

Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn
        340   345   350

Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu
    355   360   365

Thr

<210> 2967
<211> 323
<212> PRT
<213> Homo sapiens

<400> 2967

Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr Leu Ser Pro Ala Val Pro
1   5   10   15

Phe Ser Gly Thr Ile Gln Gly Gly Leu Gln Asp Gly Leu Gln Ile Thr
                20   25   30

Val Asn Gly Thr Val Leu Ser Ser Ser Gly Thr Arg Phe Ala Val Asn
            35   40   45

Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile Ala Phe His Phe Asn Pro
        50   55   60

Arg Phe Glu Asp Gly Gly Tyr Val Val Cys Asn Thr Arg Gln Asn Gly
65   70   75   80

Ser Trp Gly Pro Glu Glu Arg Arg Thr His Met Pro Phe Gln Lys Gly
                85   90   95

Met Pro Phe Asp Leu Cys Phe Leu Val Gln Ser Ser Asp Phe Lys Val
            100   105   110

Met Val Asn Gly Ile Leu Phe Val Gln Tyr Phe His Arg Val Pro Phe
        115   120   125

His Arg Val Asp Thr Ile Phe Val Asn Gly Ser Val Gln Leu Ser Tyr
    130   135   140

Ile Ser Phe Gln Pro Pro Gly Val Trp Pro Ala Asn Pro Ala Pro Ile
145   150   155   160

Thr Gln Thr Val Ile His Thr Val Gln Ser Ala Pro Gly Gln Met Phe
                165   170   175

Ser Thr Pro Ala Ile Pro Pro Met Met Tyr Pro His Pro Ala Tyr Pro
            180   185   190

Met Pro Phe Ile Thr Thr Ile Leu Gly Gly Leu Tyr Pro Ser Lys Ser
            195   200   205

Ile Leu Leu Ser Gly Thr Val Leu Pro Ser Ala Gln Arg Phe His Ile
    210   215   220

1349

```
Asn Leu Cys Ser Gly Asn His Ile Ala Phe His Leu Asn Leu Arg Phe
225                 230             235                 240

Asp Glu Asn Ala Val Val Arg Asn Thr Gln Ile Asp Asn Ser Trp Gly
                245             250                 255

Ser Glu Glu Arg Ser Leu Pro Arg Lys Met Pro Phe Val Arg Gly Gln
            260             265                 270

Ser Phe Ser Val Trp Ile Leu Cys Gly Ala His Cys Leu Lys Val Ala
        275             280             285                    .

Val Asp Gly Gln His Leu Phe Glu Tyr Tyr His Arg Leu Arg Asn Leu
    290             295             300

Pro Thr Ile Asn Arg Leu Glu Val Gly Gly Asp Ile Gln Leu Thr His
305             310             315                 320

Val Gln Thr
```

```
<210>  2968
<211>  1866
<212>  PRT
<213>  Homo sapiens

<400>  2968
```

```
Met Asp Pro Val Gly Leu Gln Leu Gly Asn Lys Asn Leu Trp Ser Cys
1               5               10                  15

Leu Val Arg Leu Leu Thr Lys Asp Pro Glu Trp Leu Asn Ala Lys Met
        20              25                  30

Lys Phe Phe Leu Pro Asn Thr Asp Leu Asp Ser Arg Asn Glu Thr Leu
        35              40                  45

Asp Pro Glu Gln Arg Val Ile Leu Gln Leu Asn Lys Leu His Val Gln
    50              55                  60

Gly Ser Asp Thr Trp Gln Ser Phe Ile His Cys Val Cys Met Gln Leu
65              70              75                  80

Glu Val Pro Leu Asp Leu Glu Val Leu Leu Ser Thr Phe Gly Tyr
            85              90                  95
```

Asp Asp Gly Phe Thr Ser Gln Leu Gly Ala Glu Gly Lys Ser Gln Pro
        100   105   110

Glu Ser Gln Leu His His Gly Leu Lys Arg Pro His Gln Ser Cys Gly
        115   120   125

Ser Ser Pro Arg Arg Lys Gln Cys Lys Lys Gln Gln Leu Glu Leu Ala
    130   135   140

Lys Lys Tyr Leu Gln Leu Leu Arg Thr Ser Ala Gln Gln Arg Tyr Arg
145   150   155   160

Ser Gln Ile Pro Gly Ser Gly Gln Pro His Ala Phe His Gln Val Tyr
            165   170   175

Val Pro Pro Ile Leu Arg Arg Ala Thr Ala Ser Leu Asp Thr Pro Glu
            180   185   190

Gly Ala Ile Met Gly Asp Val Lys Val Glu Asp Gly Ala Asp Val Ser
        195   200   205

Ile Ser Asp Leu Phe Asn Thr Arg Val Asn Lys Gly Pro Arg Val Thr
    210   215   220

Val Leu Leu Gly Lys Ala Gly Met Gly Lys Thr Thr Leu Ala His Arg
225   230   235   240

Leu Cys Gln Lys Trp Ala Glu Gly His Leu Asn Cys Phe Gln Ala Leu
            245   250   255

Phe Leu Phe Glu Phe Arg Gln Leu Asn Leu Ile Thr Arg Phe Leu Thr
            260   265   270

Pro Ser Glu Leu Leu Phe Asp Leu Tyr Leu Ser Pro Glu Ser Asp His
    275   280   285

Asp Thr Val Phe Gln Tyr Leu Glu Lys Asn Ala Asp Gln Val Leu Leu
    290   295   300

Ile Phe Asp Gly Leu Asp Glu Ala Leu Gln Pro Met Gly Pro Asp Gly
305   310   315   320

Pro Gly Pro Val Leu Thr Leu Phe Ser His Leu Cys Asn Gly Thr Leu
            325   330   335

Leu Pro Gly Cys Arg Val Met Ala Thr Ser Arg Pro Gly Lys Leu Pro

1351

                340   345   350

    Ala Cys Leu Pro Ala Glu Ala Ala Met Val His Met Leu Gly Phe Asp
            355   360   365

    Gly Pro Arg Val Glu Glu Tyr Val Asn His Phe Phe Ser Ala Gln Pro
        370   375   380

    Ser Arg Glu Gly Ala Leu Val Glu Leu Gln Thr Asn Gly Arg Leu Arg
    385   390   395   400

    Ser Leu Cys Ala Val Pro Ala Leu Cys Gln Val Ala Cys Leu Cys Leu
                405   410   415

    His His Leu Leu Pro Asp His Ala Pro Gly Gln Ser Val Ala Leu Leu
            420   425   430

    Pro Asn Met Thr Gln Leu Tyr Met Gln Met Val Leu Ala Leu Ser Pro
            435   440   445

    Pro Gly His Leu Pro Thr Ser Ser Leu Leu Asp Leu Gly Glu Val Ala
        450   455   460

    Leu Arg Gly Leu Glu Thr Gly Lys Val Ile Phe Tyr Ala Lys Asp Ile
    465   470   475   480

    Ala Pro Pro Leu Ile Ala Phe Gly Ala Thr His Ser Leu Leu Thr Ser
                485   490   495

    Phe Cys Val Cys Thr Gly Pro Gly His Gln Gln Thr Gly Tyr Ala Phe
                500   505   510

    Thr His Leu Ser Leu Gln Glu Phe Leu Ala Ala Leu His Leu Met Ala
            515   520   525

    Ser Pro Lys Val Asn Lys Asp Thr Leu Thr Gln Tyr Val Thr Leu His
        530   535   540

    Ser Arg Trp Val Gln Arg Thr Lys Ala Arg Leu Gly Leu Ser Asp His
    545   550   555   560

    Leu Pro Thr Phe Leu Ala Gly Leu Ala Ser Cys Thr Cys Arg Pro Phe
                565   570   575

    Leu Ser His Leu Ala Gln Gly Asn Glu Asp Cys Val Gly Ala Lys Gln
            580   585   590

                                1352

```
Ala Ala Val Val Gln Val Leu Lys Lys Leu Ala Thr Arg Lys Leu Thr
        595             600             605                    .

Gly Pro Lys Val Val Glu Leu Cys His Cys Val Asp Glu Thr Gln Glu
    610             615             620

Pro Glu Leu Ala Ser Leu Thr Ala Gln Ser Leu Pro Tyr Gln Leu Pro
625             630             635                    640

Phe His Asn Phe Pro Leu Thr Cys Thr Asp Leu Ala Thr Leu Thr Asn
            645             650             655

Ile Leu Glu His Arg Glu Ala Pro Ile His Leu Asp Phe Asp Gly Cys
        660             665             670

Pro Leu Glu Pro His Cys Pro Glu Ala Leu Val Gly Cys Gly Gln Ile
        675             680             685

Glu Asn Leu Ser Phe Lys Ser Arg Lys Cys Gly Asp Ala Phe Ala Glu
    690             695             700

Ala Leu Ser Arg Ser Leu Pro Thr Met Gly Arg Leu Gln Met Leu Gly
705             710             715                    720

Leu Ala Gly Ser Lys Ile Thr Ala Arg Gly Ile Ser His Leu Val Lys
            725             730             735

Ala Leu Pro Leu Cys Pro Gln Leu Lys Glu Val Ser Phe Arg Asp Asn
            740             745             750
                                .

Gln Leu Ser Asp Gln Val Val Leu Asn Ile Val Glu Val Leu Pro His
        755             760             765

Leu Pro Arg Leu Arg Lys Leu Asp Leu Ser Ser Asn Ser Ile Cys Val
    770             775             780

Ser Thr Leu Leu Cys Leu Ala Arg Val Ala Val Thr Cys Pro Thr Val
785             790             795             800

Arg Met Leu Gln Ala Arg Glu Arg Thr Ile Ile Phe Leu Leu Ser Pro
            805             810             815

Pro Thr Glu Thr Thr Ala Glu Leu Gln Arg Ala Pro Asp Leu Gln Glu
    820             825             830
```

Ser Asp Gly Gln Arg Lys Gly Ala Gln Ser Arg Ser Leu Thr Leu Arg
        835   840   845

Leu Gln Lys Cys Gln Leu Gln Val His Asp Ala Glu Ala Leu Ile Ala
    850   855   860

Leu Leu Gln Glu Gly Pro His Leu Glu Glu Val Asp Leu Ser Gly Asn
865   870   875   880

Gln Leu Glu Asp Glu Gly Cys Arg Leu Met Ala Glu Ala Ala Ser Gln
                885   890   895

Leu His Ile Ala Arg Lys Leu Asp Leu Ser Asp Asn Gly Leu Ser Val
            900   905   910

Ala Gly Val His Cys Val Leu Arg Ala Val Ser Ala Cys Trp Thr Leu
        915   920   925

Ala Glu Leu His Ile Ser Leu Gln His Lys Thr Val Ile Phe Met Phe
    930   935   940

Ala Gln Glu Pro Glu Glu Gln Lys Gly Pro Gln Glu Arg Ala Ala Phe
945   950   955   960

Leu Asp Ser Leu Met Leu Gln Met Pro Ser Glu Leu Pro Leu Ser Ser
            965   970   975

Arg Arg Met Arg Leu Thr His Cys Gly Leu Gln Glu Lys His Leu Glu
            980   985   990

Gln Leu Cys Lys Ala Leu Gly Gly Ser Cys His Leu Gly His Leu His
        995   1000   1005

Leu Asp Phe Ser Gly Asn Ala Leu Gly Asp Glu Gly Ala Ala Arg
    1010   1015   1020

Leu Ala Gln Leu Leu Pro Gly Leu Gly Ala Leu Gln Ser Leu Asn
    1025   1030   1035

Leu Ser Glu Asn Gly Leu Ser Leu Asp Ala Val Leu Gly Leu Val
    1040   1045   1050

Arg Cys Phe Ser Thr Leu Gln Trp Leu Phe Arg Leu Asp Ile Ser
    1055   1060   1065

1354

Phe Glu Ser Gln His Ile Leu Leu Arg Gly Asp Lys Thr Ser Arg
    1070   1075   1080

Asp Met Trp Ala Thr Gly Ser Leu Pro Asp Phe Pro Ala Ala Ala
    1085   1090   1095

Lys Phe Leu Gly Phe Arg Gln Arg Cys Ile Pro Arg Ser Leu Cys
    1100   1105   1110

Leu Ser Glu Cys Pro Leu Glu Pro Pro Ser Leu Thr Arg Leu Cys
    1115   1120   1125

Ala Thr Leu Lys Asp Cys Pro Gly Pro Leu Glu Leu Gln Leu Ser
    1130   1135   1140

Cys Glu Phe Leu Ser Asp Gln Ser Leu Glu Thr Leu Leu Asp Cys
    1145   1150   1155

Leu Pro Gln Leu Pro Gln Leu Ser Leu Leu Gln Leu Ser Gln Thr
    1160   1165   1170

Gly Leu Ser Pro Lys Ser Pro Phe Leu Leu Ala Asn Thr Leu Ser
    1175   1180   1185

Leu Cys Pro Arg Val Lys Lys Val Asp Leu Arg Ser Leu His His
    1190   1195   1200

Ala Thr Leu His Phe Arg Ser Asn Glu Glu Glu Glu Gly Val Cys
    1205   1210   1215

Cys Gly Arg Phe Thr Gly Cys Ser Leu Ser Gln Glu His Val Glu
    1220   1225   1230

Ser Leu Cys Trp Leu Leu Ser Lys Cys Lys Asp Leu Ser Gln Val
    1235   1240   1245

Asp Leu Ser Ala Asn Leu Leu Gly Asp Ser Gly Leu Arg Cys Leu
    1250   1255   1260

Leu Glu Cys Leu Pro Gln Val Pro Ile Ser Gly Leu Leu Asp Leu
    1265   1270   1275

Ser His Asn Ser Ile Ser Gln Glu Ser Ala Leu Tyr Leu Leu Glu
    1280   1285   1290

Thr Leu Pro Ser Cys Pro Arg Val Arg Glu Ala Ser Val Asn Leu

```
        1295                  1300                  1305


Gly Ser Glu Gln Ser Phe Arg Ile His Phe Ser Arg Glu Asp Gln
    1310              1315              1320


Ala Gly Lys Thr Leu Arg Leu Ser Glu Cys Ser Phe Arg Pro Glu
    1325              1330              1335


His Val Ser Arg Leu Ala Thr Gly Leu Ser Lys Ser Leu Gln Leu
    1340              1345              1350


Thr Glu Leu Thr Leu Thr Gln Cys Cys Leu Gly Gln Lys Gln Leu
    1355              1360              1365


Ala Ile Leu Leu Ser Leu Val Gly Arg Pro Ala Gly Leu Phe Ser
    1370              1375              1380


Leu Arg Val Gln Glu Pro Trp Ala Asp Arg Ala Arg Val Leu Ser
    1385              1390              1395


Leu Leu Glu Val Cys Ala Gln Ala Ser Gly Ser Val Thr Glu Ile
    1400              1405              1410


Ser Ile Ser Glu Thr Gln Gln Gln Leu Cys Val Gln Leu Glu Phe
    1415              1420              1425


Pro Arg Gln Glu Glu Asn Pro Glu Ala Val Ala Leu Arg Leu Ala
    1430              1435              1440


His Cys Asp Leu Gly Ala His His Ser Leu Leu Val Gly Gln Leu
    1445              1450              1455


Met Glu Thr Cys Ala Arg Leu Gln Gln Leu Ser Leu Ser Gln Val
    1460              1465              1470


Asn Leu Cys Glu Asp Asp Asp Ala Ser Ser Leu Leu Leu Gln Ser
    1475              1480              1485


Leu Leu Leu Ser Leu Ser Glu Leu Lys Thr Phe Arg Leu Thr Ser
    1490              1495              1500


Ser Cys Val Ser Thr Glu Gly Leu Ala His Leu Ala Ser Gly Leu
    1505              1510              1515


Gly His Cys His His Leu Glu Glu Leu Asp Leu Ser Asn Asn Gln
    1520              1525              1530
```

Phe Asp Glu Glu Gly Thr Lys Ala Leu Met Arg Ala Leu Glu Gly
    1535   1540   1545

Lys Trp Met Leu Lys Arg Leu Asp Leu Ser His Leu Leu Leu Asn
    1550   1555   1560

Ser Ser Thr Leu Ala Leu Leu Thr His Arg Leu Ser Gln Met Thr
    1565   1570   1575

Cys Leu Gln Ser Leu Arg Leu Asn Arg Asn Ser Ile Gly Asp Val
    1580   1585   1590

Gly Cys Cys His Leu Ser Glu Ala Leu Arg Ala Ala Thr Ser Leu
    1595   1600   1605

Glu Glu Leu Asp Leu Ser His Asn Gln Ile Gly Asp Ala Gly Val
    1610   1615   1620

Gln His Leu Ala Thr Ile Leu Pro Gly Leu Pro Glu Leu Arg Lys
    1625   1630   1635

Ile Asp Leu Ser Gly Asn Ser Ile Ser Ser Ala Gly Gly Val Gln
    1640   1645   1650

Leu Ala Glu Ser Leu Val Leu Cys Arg Arg Leu Glu Glu Leu Met
    1655   1660   1665

Leu Gly Cys Asn Ala Leu Gly Asp Pro Thr Ala Leu Gly Leu Ala
    1670   1675   1680

Gln Glu Leu Pro Gln His Leu Arg Val Leu His Leu Pro Phe Ser
    1685   1690   1695

His Leu Gly Pro Gly Gly Ala Leu Ser Leu Ala Gln Ala Leu Asp
    1700   1705   1710

Gly Ser Pro His Leu Glu Glu Ile Ser Leu Ala Glu Asn Asn Leu
    1715   1720   1725

Ala Gly Gly Val Leu Arg Phe Cys Met Glu Leu Pro Leu Leu Arg
    1730   1735   1740

Gln Ile Asp Leu Val Ser Cys Lys Ile Asp Asn Gln Thr Ala Lys
    1745   1750   1755

```
Leu Leu  Thr Ser Ser Phe Thr  Ser Cys Pro Ala Leu  Glu Val Ile
    1760                 1765              1770

Leu Leu  Ser Trp Asn Leu Leu  Gly Asp Glu Ala Ala  Ala Glu Leu
    1775                 1780              1785

Ala Gln  Val Leu Pro Lys Met  Gly Arg Leu Lys Arg  Val Asp Leu
    1790                 1795              1800

Glu Lys  Asn Gln Ile Thr Ala  Leu Gly Ala Trp Leu  Leu Ala Glu
    1805                 1810              1815

Gly Leu  Ala Gln Gly Ser Ser  Ile Gln Val Ile Arg  Leu Trp Asn
    1820                 1825              1830

Asn Pro  Ile Pro Cys Asp Met  Ala Gln His Leu Lys  Ser Gln Glu
    1835                 1840              1845

Pro Arg  Leu Asp Phe Ala Phe  Phe Asp Asn Gln Pro  Gln Ala Pro
    1850                 1855              1860

Trp Gly  Thr
    1865
```

```
<210>  2969
<211>  547
<212>  PRT
<213>  Homo sapiens

<400>  2969

Met Ala Thr Met Val Pro Ser Val Leu Trp Pro Arg Ala Cys Trp Thr
1               5               10              15

Leu Leu Val Cys Cys Leu Leu Thr Pro Gly Val Gln Gly Gln Glu Phe
            20              25              30

Leu Leu Arg Val Glu Pro Gln Asn Pro Val Leu Ser Ala Gly Gly Ser
        35              40              45

Leu Phe Val Asn Cys Ser Thr Asp Cys Pro Ser Ser Glu Lys Ile Ala
    50              55              60

Leu Glu Thr Ser Leu Ser Lys Glu Leu Val Ala Ser Gly Met Gly Trp
65              70              75              80

Ala Ala Phe Asn Leu Ser Asn Val Thr Gly Asn Ser Arg Ile Leu Cys
```

                        85   90   95

      Ser Val Tyr Cys Asn Gly Ser Gln Ile Thr Gly Ser Ser Asn Ile Thr
                    100   105   110

      Val Tyr Gly Leu Pro Glu Arg Val Glu Leu Ala Pro Leu Pro Pro Trp
              115   120   125

      Gln Pro Val Gly Gln Asn Phe Thr Leu Arg Cys Gln Val Glu Gly Gly
          130   135   140

      Ser Pro Arg Thr Ser Leu Thr Val Val Leu Leu Arg Trp Glu Glu Glu
      145   150   155   160

      Leu Ser Arg Gln Pro Ala Val Glu Glu Pro Ala Glu Val Thr Ala Thr
                    165   170   175

      Val Leu Ala Ser Arg Asp Asp His Gly Ala Pro Phe Ser Cys Arg Thr
                    180   185   190

      Glu Leu Asp Met Gln Pro Gln Gly Leu Gly Leu Phe Val Asn Thr Ser
              195   200   205

      Ala Pro Arg Gln Leu Arg Thr Phe Val Leu Pro Val Thr Pro Pro Arg
          210   215   220

      Leu Val Ala Pro Arg Phe Leu Glu Val Glu Thr Ser Trp Pro Val Asp
      225   230   235   240

      Cys Thr Leu Asp Gly Leu Phe Pro Ala Ser Glu Ala Gln Val Tyr Leu
                    245   250   255

      Ala Leu Gly Asp Gln Met Leu Asn Ala Thr Val Met Asn His Gly Asp
                    260   265   270

      Thr Leu Thr Ala Thr Ala Thr Ala Thr Ala Arg Ala Asp Gln Glu Gly
                    275   280   285

      Ala Arg Glu Ile Val Cys Asn Val Thr Leu Gly Gly Glu Arg Arg Glu
          290   295   300

      Ala Arg Glu Asn Leu Thr Val Phe Ser Phe Leu Gly Pro Ile Val Asn
      305   310   315   320

      Leu Ser Glu Pro Thr Ala His Glu Gly Ser Thr Val Thr Val Ser Cys
                    325   330   335

                                   1359

```
Met Ala Gly Ala Arg Val Gln Val Thr Leu Asp Gly Val Pro Ala Ala
            340             345             350


Ala Pro Gly Gln Pro Ala Gln Leu Gln Leu Asn Ala Thr Glu Ser Asp
            355             360             365


Asp Gly Arg Ser Phe Phe Cys Ser Ala Thr Leu Glu Val Asp Gly Glu
        370             375             380


Phe Leu His Arg Asn Ser Ser Val Gln Leu Arg Val Leu Tyr Gly Pro
385             390             395             400


Lys Ile Asp Arg Ala Thr Cys Pro Gln His Leu Lys Trp Lys Asp Lys
            405             410             415


Thr Arg His Val Leu Gln Cys Gln Ala Arg Gly Asn Pro Tyr Pro Glu
            420             425             430


Leu Arg Cys Leu Lys Glu Gly Ser Ser Arg Glu Val Pro Val Gly Ile
            435             440             445


Pro Phe Phe Val Asn Val Thr His Asn Gly Thr Tyr Gln Cys Gln Ala
    450             455             460


Ser Ser Ser Arg Gly Lys Tyr Thr Leu Val Val Val Met Asp Ile Glu
465             470             475             480


Ala Gly Ser Ser His Phe Val Pro Val Phe Val Ala Val Leu Leu Thr
            485             490             495


Leu Gly Val Val Thr Ile Val Leu Ala Leu Met Tyr Val Phe Arg Glu
            500             505             510


His Gln Arg Ser Gly Ser Tyr His Val Arg Glu Glu Ser Thr Tyr Leu
            515             520             525


Pro Leu Thr Ser Met Gln Pro Thr Glu Ala Met Gly Glu Glu Pro Ser
            530             535             540


Arg Ala Glu
545


<210>   2970
<211>   260
<212>   PRT
```

<213> Homo sapiens

<400> 2970

```
Met Arg Pro Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg
1               5               10              15

Ala Leu Ser Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile
            20              25              30

Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg
        35              40              45

Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr
    50              55              60

Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly
65              70              75              80

Gln Ala Phe Ser Phe Glu Ala Gln Gly Gly Leu Ala Asn Ile Ala Ile
                85              90              95

Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln
            100             105             110

Ala Thr Asn Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val
        115             120             125

Glu Leu Gly Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe
    130             135             140

Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr
145             150             155             160

Glu Gly Val Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe
                165             170             175

His Lys Phe His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr
            180             185             190

Asp Cys Arg Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His
        195             200             205

Trp Glu Ala Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val
    210             215             220

Leu Cys Ala Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly
```

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225   230   235   240

</div>

Thr Val Leu Ile Ile Lys Ser Leu Arg Ser Gly His Asp Pro Arg Ala
                245   250   255

Gln Gly Thr Leu
            260

<210> 2971
<211> 495
<212> PRT
<213> Homo sapiens

<400> 2971

Met Pro Met Gly Ser Leu Gln Pro Leu Ala Thr Leu Tyr Leu Leu Gly
1   5   10   15

Met Leu Val Ala Ser Cys Leu Gly Arg Leu Ser Trp Tyr Asp Pro Asp
            20   25   30

Phe Gln Ala Arg Leu Thr Arg Ser Asn Ser Lys Cys Gln Gly Gln Leu
        35   40   45

Glu Val Tyr Leu Lys Asp Gly Trp His Met Val Cys Ser Gln Ser Trp
    50   55   60

Gly Arg Ser Ser Lys Gln Trp Glu Asp Pro Ser Gln Ala Ser Lys Val
65   70   75   80

Cys Gln Arg Leu Asn Cys Gly Val Pro Leu Ser Leu Gly Pro Phe Leu
                85   90   95

Val Thr Tyr Thr Pro Gln Ser Ser Ile Ile Cys Tyr Gly Gln Leu Gly
            100   105   110

Ser Phe Ser Asn Cys Ser His Ser Arg Asn Asp Met Cys His Ser Leu
        115   120   125

Gly Leu Thr Cys Leu Glu Pro Gln Lys Thr Thr Pro Pro Thr Thr Arg
    130   135   140

Pro Pro Pro Thr Thr Thr Pro Glu Pro Thr Ala Pro Pro Arg Leu Gln
145   150   155   160

Leu Val Ala Gln Ser Gly Gly Gln His Cys Ala Gly Val Val Glu Phe
                165   170   175

<div align="center">

1362

</div>

Tyr Ser Gly Ser Leu Gly Gly Thr Ile Ser Tyr Glu Ala Gln Asp Lys
        180   185   190

Thr Gln Asp Leu Glu Asn Phe Leu Cys Asn Asn Leu Gln Cys Gly Ser
        195   200   205

Phe Leu Lys His Leu Pro Glu Thr Glu Ala Gly Arg Ala Gln Asp Pro
        210   215   220

Gly Glu Pro Arg Glu His Gln Pro Leu Pro Ile Gln Trp Lys Ile Gln
225   230   235   240

Asn Ser Ser Cys Thr Ser Leu Glu His Cys Phe Arg Lys Ile Lys Pro
                245   250   255

Gln Lys Ser Gly Arg Val Leu Ala Leu Leu Cys Ser Gly Phe Gln Pro
                260   265   270

Lys Val Gln Ser Arg Leu Val Gly Gly Ser Ser Ile Cys Glu Gly Thr
                275   280   285

Val Glu Val Arg Gln Gly Ala Gln Trp Ala Ala Leu Cys Asp Ser Ser
        290   295   300

Ser Ala Arg Ser Ser Leu Arg Trp Glu Glu Val Cys Arg Glu Gln Gln
305   310   315   320

Cys Gly Ser Val Asn Ser Tyr Arg Val Leu Asp Ala Gly Asp Pro Thr
                325   330   335

Ser Arg Gly Leu Phe Cys Pro His Gln Lys Leu Ser Gln Cys His Glu
                340   345   350

Leu Trp Glu Arg Asn Ser Tyr Cys Lys Lys Val Phe Val Thr Cys Gln
        355   360   365

Asp Pro Asn Pro Ala Gly Leu Ala Ala Gly Thr Val Ala Ser Ile Ile
        370   375   380

Leu Ala Leu Val Leu Leu Val Val Leu Leu Val Val Cys Gly Pro Leu
385   390   395   400

Ala Tyr Lys Lys Leu Val Lys Lys Phe Arg Gln Lys Lys Gln Arg Gln
        405   410   415

```
Trp Ile Gly Pro Thr Gly Met Asn Gln Asn Met Ser Phe His Arg Asn
        420                 425             430

His Thr Ala Thr Val Arg Ser His Ala Glu Asn Pro Thr Ala Ser His
        435                 440             445

Val Asp Asn Glu Tyr Ser Gln Pro Pro Arg Asn Ser Arg Leu Ser Ala
    450                 455             460

Tyr Pro Ala Leu Glu Gly Val Leu His Arg Ser Ser Met Gln Pro Asp
465                 470             475                 480

Asn Ser Ser Asp Ser Asp Tyr Asp Leu His Gly Ala Gln Arg Leu
            485             490             495
```

```
<210>  2972
<211>  130
<212>  PRT
<213>  Homo sapiens

<400>  2972

Lys Val Phe Glu Arg Cys Glu Leu Ala Arg Thr Leu Lys Arg Leu Gly
1               5               10              15

Met Asp Gly Tyr Arg Gly Ile Ser Leu Ala Asn Trp Met Cys Leu Ala
            20              25              30

Lys Trp Glu Ser Gly Tyr Asn Thr Arg Ala Thr Asn Tyr Asn Ala Gly
        35              40              45

Asp Arg Ser Thr Asp Tyr Gly Ile Phe Gln Ile Asn Ser Arg Tyr Trp
    50              55              60

Cys Asn Asp Gly Lys Thr Pro Gly Ala Val Asn Ala Cys His Leu Ser
65              70              75              80

Cys Ser Ala Leu Leu Gln Asp Asn Ile Ala Asp Ala Val Ala Cys Ala
            85              90              95

Lys Arg Val Val Arg Asp Pro Gln Gly Ile Arg Ala Trp Val Ala Trp
            100             105             110

Arg Asn Arg Cys Gln Asn Arg Asp Val Arg Gln Tyr Val Gln Gly Cys
        115             120             125

Gly Val
    130
```

<210> 2973
<211> 491
<212> PRT
<213> Homo sapiens

<400> 2973

Met Asn Pro Ala Ala Glu Ala Glu Phe Asn Ile Leu Leu Ala Thr Asp
1   5   10   15

Ser Tyr Lys Val Thr His Tyr Lys Gln Tyr Pro Pro Asn Thr Ser Lys
            20   25   30

Val Tyr Ser Tyr Phe Glu Cys Arg Glu Lys Lys Thr Glu Asn Ser Lys
            35   40   45

Leu Arg Lys Val Lys Tyr Glu Glu Thr Val Phe Tyr Gly Leu Gln Tyr
        50   55   60

Ile Leu Asn Lys Tyr Leu Lys Gly Lys Val Val Thr Lys Glu Lys Ile
65   70   75   80

Gln Glu Ala Lys Asp Val Tyr Lys Glu His Phe Gln Asp Asp Val Phe
                85   90   95

Asn Glu Lys Gly Trp Asn Tyr Ile Leu Glu Lys Tyr Asp Gly His Leu
            100   105   110

Pro Ile Glu Ile Lys Ala Val Pro Glu Gly Phe Val Ile Pro Arg Gly
        115   120   125

Asn Val Leu Phe Thr Val Glu Asn Thr Asp Pro Glu Cys Tyr Trp Leu
    130   135   140

Thr Asn Trp Ile Glu Thr Ile Leu Val Gln Ser Trp Tyr Pro Ile Thr
145   150   155   160

Val Ala Thr Asn Ser Arg Glu Gln Lys Lys Ile Leu Ala Lys Tyr Leu
                165   170   175

Leu Glu Thr Ser Gly Asn Leu Asp Gly Leu Glu Tyr Lys Leu His Asp
            180   185   190

Phe Gly Tyr Arg Gly Val Ser Ser Gln Glu Thr Ala Gly Ile Gly Ala
            195   200   205

Ser Ala His Leu Val Asn Phe Lys Gly Thr Asp Thr Val Ala Gly Leu
    210   215   220

Ala Leu Ile Lys Lys Tyr Tyr Gly Thr Lys Asp Pro Val Pro Gly Tyr
225   230   235   240

Ser Val Pro Ala Ala Glu His Ser Thr Ile Thr Ala Trp Gly Lys Asp
            245   250   255

His Glu Lys Asp Ala Phe Glu His Ile Val Thr Gln Phe Ser Ser Val
            260   265   270

Pro Val Ser Val Val Ser Asp Ser Tyr Asp Ile Tyr Asn Ala Cys Glu
        275   280   285

Lys Ile Trp Gly Glu Asp Leu Arg His Leu Ile Val Ser Arg Ser Thr
    290   295   300

Gln Ala Pro Leu Ile Ile Arg Pro Asp Ser Gly Asn Pro Leu Asp Thr
305   310   315   320

Val Leu Lys Val Leu Glu Ile Leu Gly Lys Lys Phe Pro Val Thr Glu
            325   330   335

Asn Ser Lys Gly Tyr Lys Leu Leu Pro Pro Tyr Leu Arg Val Ile Gln
            340   345   350

Gly Asp Gly Val Asp Ile Asn Thr Leu Gln Glu Ile Val Glu Gly Met
            355   360   365

Lys Gln Lys Met Trp Ser Ile Glu Asn Ile Ala Phe Gly Ser Gly Gly
    370   375   380

Gly Leu Leu Gln Lys Leu Thr Arg Asp Leu Leu Asn Cys Ser Phe Lys
385   390   395   400

Cys Ser Tyr Val Val Thr Asn Gly Leu Gly Ile Asn Val Phe Lys Asp
            405   410   415

Pro Val Ala Asp Pro Asn Lys Arg Ser Lys Lys Gly Arg Leu Ser Leu
            420   425   430

His Arg Thr Pro Ala Gly Asn Phe Val Thr Leu Glu Glu Gly Lys Gly
            435   440   445

Asp Leu Glu Glu Tyr Gly Gln Asp Leu Leu His Thr Val Phe Lys Asn

                450   455   460

Gly Lys Val Thr Lys Ser Tyr Ser Phe Asp Glu Ile Arg Lys Asn Ala
465   470   475   480

Gln Leu Asn Ile Glu Leu Glu Ala Ala His His
                485   490

<210> 2974
<211> 862
<212> PRT
<213> Homo sapiens

<400> 2974

Met Glu Arg Ala Glu Ser Ser Ser Thr Glu Pro Ala Lys Ala Ile Lys
1   5   10   15

Pro Ile Asp Arg Lys Ser Val His Gln Ile Cys Ser Gly Gln Val Val
            20   25   30

Leu Ser Leu Ser Thr Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp
        35   40   45

Ala Gly Ala Thr Asn Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp
        50   55   60

Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe
65   70   75   80

Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala
                85   90   95

Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser
            100   105   110

Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Ala Ser
        115   120   125

Ala Lys Val Gly Thr Arg Leu Met Phe Asp His Asn Gly Lys Ile Ile
        130   135   140

Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Thr Thr Val Ser Val Gln
145   150   155   160

Gln Leu Phe Ser Thr Leu Pro Val Arg His Lys Glu Phe Gln Arg Asn
                165   170   175

Ile Lys Lys Glu Tyr Ala Lys Met Val Gln Val Leu His Ala Tyr Cys
        180   185   190

Ile Ile Ser Ala Gly Ile Arg Val Ser Cys Thr Asn Gln Leu Gly Gln
        195   200   205

Gly Lys Arg Gln Pro Val Val Cys Thr Gly Gly Ser Pro Ser Ile Lys
    210   215   220

Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile
225   230   235   240

Pro Phe Val Gln Leu Pro Pro Ser Asp Ser Val Cys Glu Glu Tyr Gly
            245   250   255

Leu Ser Cys Ser Asp Ala Leu His Asn Leu Phe Tyr Ile Ser Gly Phe
        260   265   270

Ile Ser Gln Cys Thr His Gly Val Gly Arg Ser Ser Thr Asp Arg Gln
    275   280   285

Phe Phe Phe Ile Asn Arg Arg Pro Cys Asp Pro Ala Lys Val Cys Arg
    290   295   300

Leu Val Asn Glu Val Tyr His Met Tyr Asn Arg His Gln Tyr Pro Phe
305   310   315   320

Val Val Leu Asn Ile Ser Val Asp Ser Glu Cys Val Asp Ile Asn Val
            325   330   335

Thr Pro Asp Lys Arg Gln Ile Leu Leu Gln Glu Glu Lys Leu Leu Leu
            340   345   350

Ala Val Leu Lys Thr Ser Leu Ile Gly Met Phe Asp Ser Asp Val Asn
        355   360   365

Lys Leu Asn Val Ser Gln Gln Pro Leu Leu Asp Val Glu Gly Asn Leu
    370   375   380

Ile Lys Met His Ala Ala Asp Leu Glu Lys Pro Met Val Glu Lys Gln
385   390   395   400

Asp Gln Ser Pro Ser Leu Arg Thr Gly Glu Glu Lys Lys Asp Val Ser
                405   410   415

1368

Ile Ser Arg Leu Arg Glu Ala Phe Ser Leu Arg His Thr Thr Glu Asn
            420   425   430

Lys Pro His Ser Pro Lys Thr Pro Glu Pro Arg Arg Ser Pro Leu Gly
            435   440   445

Gln Lys Arg Gly Met Leu Ser Ser Ser Thr Ser Gly Ala Ile Ser Asp
        450   455   460

Lys Gly Val Leu Arg Pro Gln Lys Glu Ala Val Ser Ser Ser His Gly
465   470   475   480

Pro Ser Asp Pro Thr Asp Arg Ala Glu Val Glu Lys Asp Ser Gly His
            485   490   495

Gly Ser Thr Ser Val Asp Ser Glu Gly Phe Ser Ile Pro Asp Thr Gly
            500   505   510

Ser His Cys Ser Ser Glu Tyr Ala Ala Ser Ser Pro Gly Asp Arg Gly
            515   520   525

Ser Gln Glu His Val Asp Ser Gln Glu Lys Ala Pro Glu Thr Asp Asp
        530   535   540

Ser Phe Ser Asp Val Asp Cys His Ser Asn Gln Glu Asp Thr Gly Cys
545   550   555   560

Lys Phe Arg Val Leu Pro Gln Pro Thr Asn Leu Ala Thr Pro Asn Thr
            565   570   575

Lys Arg Phe Lys Lys Glu Glu Ile Leu Ser Ser Ser Asp Ile Cys Gln
            580   585   590

Lys Leu Val Asn Thr Gln Asp Met Ser Ala Ser Gln Val Asp Val Ala
            595   600   605

Val Lys Ile Asn Lys Lys Val Val Pro Leu Asp Phe Ser Met Ser Ser
    610   615   620

Leu Ala Lys Arg Ile Lys Gln Leu His His Glu Ala Gln Gln Ser Glu
625   630   635   640

Gly Glu Gln Asn Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu
            645   650   655

Asn Gln Ala Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Thr Met

```
              660                          665                        670

     Phe Ala Glu Met Glu Ile Ile Gly Gln Phe Asn Leu Gly Phe Ile Ile
             675                          680                      685

     Thr Lys Leu Asn Glu Asp Ile Phe Ile Val Asp Gln His Ala Thr Asp
             690                          695                      700

     Glu Lys Tyr Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Gly
     705                          710                      715        720

     Gln Arg Leu Ile Ala Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu
                     725                      730                  735

     Ala Val Leu Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp
                     740                      745                  750

     Phe Val Ile Asp Glu Asn Ala Pro Val Thr Glu Arg Ala Lys Leu Ile
                 755                      760                  765

     Ser Leu Pro Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Val Asp
             770                      775                  780

     Glu Leu Ile Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro
     785                      790                  795                800

     Ser Arg Val Lys Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val
                     805                      810                  815

     Met Ile Gly Thr Ala Leu Asn Thr Ser Glu Met Lys Lys Leu Ile Thr
                     820                      825                  830

     His Met Gly Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro
             835                      840                  845

     Thr Met Arg His Ile Ala Asn Leu Gly Val Ile Ser Gln Asn
     850                      855                  860
```

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<210>   2975
<211>   1256
<212>   PRT
<213>   Homo sapiens

<400>   2975

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
1                 5                      10                      15
```

```
Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Gly
            20                  25                  30

Leu Thr Thr Ala Lys Met Pro Ser Val Pro Leu Ser Ser Asp Pro Leu
            35                  40                  45

Pro Thr His Thr Thr Ala Phe Ser Pro Ala Ser Thr Phe Glu Arg Glu
    50                  55                  60

Asn Asp Phe Ser Glu Thr Thr Thr Ser Leu Ser Pro Asp Asn Thr Ser
65                  70                  75                  80

Thr Gln Val Ser Pro Asp Ser Leu Asp Asn Ala Ser Ala Phe Asn Thr
            85                  90                  95

Thr Gly Val Ser Ser Val Gln Thr Pro His Leu Pro Thr His Ala Asp
            100                 105                 110

Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser Gly Ser
    115                 120                 125

Ala Ala Asn Ala Lys Leu Asn Pro Thr Pro Gly Ser Asn Ala Ile Ser
    130                 135                 140

Asp Ala Tyr Leu Asn Ala Ser Glu Thr Thr Thr Leu Ser Pro Ser Gly
145                 150                 155                 160

Ser Ala Val Ile Ser Thr Thr Thr Ile Ala Thr Thr Pro Ser Lys Pro
            165                 170                 175

Thr Cys Asp Glu Lys Tyr Ala Asn Ile Thr Val Asp Tyr Leu Tyr Asn
            180                 185                 190

Lys Glu Thr Lys Leu Phe Thr Ala Lys Leu Asn Val Asn Glu Asn Val
    195                 200                 205

Glu Cys Gly Asn Asn Thr Cys Thr Asn Asn Glu Val His Asn Leu Thr
    210                 215                 220

Glu Cys Lys Asn Ala Ser Val Ser Ile Ser His Asn Ser Cys Thr Ala
225                 230                 235                 240

Pro Asp Lys Thr Leu Ile Leu Asp Val Pro Pro Gly Val Glu Lys Phe
            245                 250                 255
```

Gln Leu His Asp Cys Thr Gln Val Glu Lys Ala Asp Thr Thr Ile Cys
        260   265   270

Leu Lys Trp Lys Asn Ile Glu Thr Phe Thr Cys Asp Thr Gln Asn Ile
        275   280   285

Thr Tyr Arg Phe Gln Cys Gly Asn Met Ile Phe Asp Asn Lys Glu Ile
    290   295   300

Lys Leu Glu Asn Leu Glu Pro Glu His Glu Tyr Lys Cys Asp Ser Glu
305   310   315   320

Ile Leu Tyr Asn Asn His Lys Phe Thr Asn Ala Ser Lys Ile Ile Lys
            325   330   335

Thr Asp Phe Gly Ser Pro Gly Glu Pro Gln Ile Ile Phe Cys Arg Ser
        340   345   350

Glu Ala Ala His Gln Gly Val Ile Thr Trp Asn Pro Pro Gln Arg Ser
        355   360   365

Phe His Asn Phe Thr Leu Cys Tyr Ile Lys Glu Thr Glu Lys Asp Cys
    370   375   380

Leu Asn Leu Asp Lys Asn Leu Ile Lys Tyr Asp Leu Gln Asn Leu Lys
385   390   395   400

Pro Tyr Thr Lys Tyr Val Leu Ser Leu His Ala Tyr Ile Ile Ala Lys
                405   410   415

Val Gln Arg Asn Gly Ser Ala Ala Met Cys His Phe Thr Thr Lys Ser
        420   425   430

Ala Pro Pro Ser Gln Val Trp Asn Met Thr Val Ser Met Thr Ser Asp
        435   440   445

Asn Ser Met His Val Lys Cys Arg Pro Pro Arg Asp Arg Asn Gly Pro
    450   455   460

His Glu Arg Tyr His Leu Glu Val Glu Ala Gly Asn Thr Leu Val Arg
465   470   475   480

Asn Glu Ser His Lys Asn Cys Asp Phe Arg Val Lys Asp Leu Gln Tyr
            485   490   495

Ser Thr Asp Tyr Thr Phe Lys Ala Tyr Phe His Asn Gly Asp Tyr Pro

1372

```
            500                    505                    510
```

Gly Glu Pro Phe Ile Leu His His Ser Thr Ser Tyr Asn Ser Lys Ala
        515   520   525

Leu Ile Ala Phe Leu Ala Phe Leu Ile Ile Val Thr Ser Ile Ala Leu
        530   535   540

Leu Val Val Leu Tyr Lys Ile Tyr Asp Leu His Lys Lys Arg Ser Cys
545   550   555   560

Asn Leu Asp Glu Gln Gln Glu Leu Val Glu Arg Asp Asp Glu Lys Gln
                565   570   575

Leu Met Asn Val Glu Pro Ile His Ala Asp Ile Leu Leu Glu Thr Tyr
                580   585   590

Lys Arg Lys Ile Ala Asp Glu Gly Arg Leu Phe Leu Ala Glu Phe Gln
        595   600   605

Ser Ile Pro Arg Val Phe Ser Lys Phe Pro Ile Lys Glu Ala Arg Lys
        610   615   620

Pro Phe Asn Gln Asn Lys Asn Arg Tyr Val Asp Ile Leu Pro Tyr Asp
625   630   635   640

Tyr Asn Arg Val Glu Leu Ser Glu Ile Asn Gly Asp Ala Gly Ser Asn
                645   650   655

Tyr Ile Asn Ala Ser Tyr Ile Asp Gly Phe Lys Glu Pro Arg Lys Tyr
                660   665   670

Ile Ala Ala Gln Gly Pro Arg Asp Glu Thr Val Asp Asp Phe Trp Arg
        675   680   685

Met Ile Trp Glu Gln Lys Ala Thr Val Ile Val Met Val Thr Arg Cys
        690   695   700

Glu Glu Gly Asn Arg Asn Lys Cys Ala Glu Tyr Trp Pro Ser Met Glu
705   710   715   720

Glu Gly Thr Arg Ala Phe Gly Asp Val Val Val Lys Ile Asn Gln His
                725   730   735

Lys Arg Cys Pro Asp Tyr Ile Ile Gln Lys Leu Asn Ile Val Asn Lys
                740   745   750

```
Lys Glu Lys Ala Thr Gly Arg Glu Val Thr His Ile Gln Phe Thr Ser
        755             760             765

Trp Pro Asp His Gly Val Pro Glu Asp Pro His Leu Leu Leu Lys Leu
    770             775             780

Arg Arg Arg Val Asn Ala Phe Ser Asn Phe Phe Ser Gly Pro Ile Val
785             790             795             800

Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Gly Ile
            805             810             815

Asp Ala Met Leu Glu Gly Leu Glu Ala Glu Asn Lys Val Asp Val Tyr
        820             825             830

Gly Tyr Val Val Lys Leu Arg Arg Gln Arg Cys Leu Met Val Gln Val
        835             840             845

Glu Ala Gln Tyr Ile Leu Ile His Gln Ala Leu Val Glu Tyr Asn Gln
850             855             860

Phe Gly Glu Thr Glu Val Asn Leu Ser Glu Leu His Pro Tyr Leu His
865             870             875             880

Asn Met Lys Lys Arg Asp Pro Pro Ser Glu Pro Ser Pro Leu Glu Ala
            885             890             895

Glu Phe Gln Arg Leu Pro Ser Tyr Arg Ser Trp Arg Thr Gln His Ile
        900             905             910

Gly Asn Gln Glu Glu Asn Lys Ser Lys Asn Arg Asn Ser Asn Val Ile
    915             920             925

Pro Tyr Asp Tyr Asn Arg Val Pro Leu Lys His Glu Leu Glu Met Ser
    930             935             940

Lys Glu Ser Glu His Asp Ser Asp Glu Ser Ser Asp Asp Asp Ser Asp
945             950             955             960

Ser Glu Glu Pro Ser Lys Tyr Ile Asn Ala Ser Phe Ile Met Ser Tyr
            965             970             975

Trp Lys Pro Glu Val Met Ile Ala Ala Gln Gly Pro Leu Lys Glu Thr
    980             985             990
```

Ile Gly Asp Phe Trp Gln Met Ile Phe Gln Arg Lys Val Lys Val Ile
        995   1000   1005

Val Met Leu Thr Glu Leu Lys His Gly Asp Gln Glu Ile Cys Ala
    1010   1015   1020

Gln Tyr Trp Gly Glu Gly Lys Gln Thr Tyr Gly Asp Ile Glu Val
    1025   1030   1035

Asp Leu Lys Asp Thr Asp Lys Ser Ser Thr Tyr Thr Leu Arg Val
    1040   1045   1050

Phe Glu Leu Arg His Ser Lys Arg Lys Asp Ser Arg Thr Val Tyr
    1055   1060   1065

Gln Tyr Gln Tyr Thr Asn Trp Ser Val Glu Gln Leu Pro Ala Glu
    1070   1075   1080

Pro Lys Glu Leu Ile Ser Met Ile Gln Val Val Lys Gln Lys Leu
    1085   1090   1095

Pro Gln Lys Asn Ser Ser Glu Gly Asn Lys His His Lys Ser Thr
    1100   1105   1110

Pro Leu Leu Ile His Cys Arg Asp Gly Ser Gln Gln Thr Gly Ile
    1115   1120   1125

Phe Cys Ala Leu Leu Asn Leu Leu Glu Ser Ala Glu Thr Glu Glu
    1130   1135   1140

Val Val Asp Ile Phe Gln Val Val Lys Ala Leu Arg Lys Ala Arg
    1145   1150   1155

Pro Gly Met Val Ser Thr Phe Glu Gln Tyr Gln Phe Leu Tyr Asp
    1160   1165   1170

Val Ile Ala Ser Thr Tyr Pro Ala Gln Asn Gly Gln Val Lys Lys
    1175   1180   1185

Asn Asn His Gln Glu Asp Lys Ile Glu Phe Asp Asn Glu Val Asp
    1190   1195   1200

Lys Val Lys Gln Asp Ala Asn Cys Val Asn Pro Leu Gly Ala Pro
    1205   1210   1215

1375

```
Glu Lys   Leu Pro Glu Ala Lys   Glu Gln Ala Glu Gly   Ser Glu Pro
    1220                1225                1230

Thr Ser   Gly Thr Glu Gly Pro   Glu His Ser Val Asn   Gly Pro Ala
    1235                1240                1245

Ser Pro   Ala Leu Asn Gln Gly   Ser
    1250                1255
```

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<210>  2976
<211>  319
<212>  PRT
<213>  Homo sapiens

<400>  2976
```

```
Met Lys Met Ala Ser Ser Leu Ala Phe Leu Leu Leu Asn Phe His Val
1               5               10              15

Ser Leu Leu Leu Val Gln Leu Leu Thr Pro Cys Ser Ala Gln Phe Ser
            20              25              30

Val Leu Gly Pro Ser Gly Pro Ile Leu Ala Met Val Gly Glu Asp Ala
        35              40              45

Asp Leu Pro Cys His Leu Phe Pro Thr Met Ser Ala Glu Thr Met Glu
    50              55              60

Leu Lys Trp Val Ser Ser Ser Leu Arg Gln Val Val Asn Val Tyr Ala
65              70              75              80

Asp Gly Lys Glu Val Glu Asp Arg Gln Ser Ala Pro Tyr Arg Gly Arg
            85              90              95

Thr Ser Ile Leu Arg Asp Gly Ile Thr Ala Gly Lys Ala Ala Leu Arg
        100             105             110

Ile His Asn Val Thr Ala Ser Asp Ser Gly Lys Tyr Leu Cys Tyr Phe
    115             120             125

Gln Asp Gly Asp Phe Tyr Glu Lys Ala Leu Val Glu Leu Lys Val Ala
    130             135             140

Ala Leu Gly Ser Asn Leu His Val Glu Val Lys Gly Tyr Glu Asp Gly
145             150             155             160

Gly Ile His Leu Glu Cys Arg Ser Thr Gly Trp Tyr Pro Gln Pro Gln
            165             170             175
```

```
Ile Gln Trp Ser Asn Ala Lys Gly Glu Asn Ile Pro Ala Val Glu Ala
            180                 185                 190

Pro Val Val Ala Asp Gly Val Gly Leu Tyr Glu Val Ala Ala Ser Val
            195                 200                 205

Ile Met Arg Gly Gly Ser Gly Glu Gly Val Ser Cys Ile Ile Arg Asn
    210                 215                 220

Ser Leu Leu Gly Leu Glu Lys Thr Ala Ser Ile Ser Ile Ala Asp Pro
225                 230                 235                 240

Phe Phe Arg Ser Ala Gln Pro Trp Ile Ala Ala Leu Ala Gly Thr Leu
            245                 250                 255

Pro Ile Leu Leu Leu Leu Leu Ala Gly Ala Ser Tyr Phe Leu Trp Arg
            260                 265                 270

Gln Gln Lys Glu Ile Thr Ala Leu Ser Ser Glu Ile Glu Ser Glu Gln
        275                 280                 285

Glu Met Lys Glu Met Gly Tyr Ala Ala Thr Glu Arg Glu Ile Ser Leu
    290                 295                 300

Arg Glu Ser Leu Gln Glu Glu Leu Lys Arg Lys Lys Ser Ser Thr
305                 310                 315
```

```
<210>  2977
<211>  240
<212>  PRT
<213>  Homo sapiens

<400>  2977
```

```
Met Leu Leu Gln Ser Gln Thr Met Gly Val Ser His Ser Phe Thr Pro
1                   5                   10                  15

Lys Gly Ile Thr Ile Pro Gln Arg Glu Lys Pro Gly His Met Tyr Gln
            20                  25                  30

Asn Glu Asp Tyr Leu Gln Asn Gly Leu Pro Thr Glu Thr Thr Val Leu
        35                  40                  45

Gly Thr Val Gln Ile Leu Cys Cys Leu Leu Ile Ser Ser Leu Gly Ala
    50                  55                  60
```

Ile Leu Val Phe Ala Pro Tyr Pro Ser His Phe Asn Pro Ala Ile Ser
65   70   75   80

Thr Thr Leu Met Ser Gly Tyr Pro Phe Leu Gly Ala Leu Cys Phe Gly
              85   90   95

Ile Thr Gly Ser Leu Ser Ile Ile Ser Gly Lys Gln Ser Thr Lys Pro
          100   105   110

Phe Asp Leu Ser Ser Leu Thr Ser Asn Ala Val Ser Ser Val Thr Ala
          115   120   125

Gly Ala Gly Leu Phe Leu Leu Ala Asp Ser Met Val Ala Leu Arg Thr
      130   135   140

Ala Ser Gln His Cys Gly Ser Glu Met Asp Tyr Leu Ser Ser Leu Pro
145   150   155   160

Tyr Ser Glu Tyr Tyr Tyr Pro Ile Tyr Glu Ile Lys Asp Cys Leu Leu
              165   170   175

Thr Ser Val Ser Leu Thr Gly Val Leu Val Val Met Leu Ile Phe Thr
              180   185   190

Val Leu Glu Leu Leu Leu Ala Ala Tyr Ser Ser Val Phe Trp Trp Lys
          195   200   205

Gln Leu Tyr Ser Asn Asn Pro Gly Ser Ser Phe Ser Ser Thr Gln Ser
      210   215   220

Gln Asp His Ile Gln Gln Val Lys Lys Ser Ser Ser Arg Ser Trp Ile
225   230   235   240

<210> 2978
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2978

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1   5   10   15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
          20   25   30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
      35   40   45

```
Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
    50                  55              60

Glu Phe Leu Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65                  70·             75                      80

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Leu
                85              90              95

Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
            100             105             110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
        115             120             125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
    130             135             140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145             150             155             160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
            165             170             175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
            180             185             190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
    195             200             205

Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210             215             220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225             230             235             240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
            245             250             255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
            260             265


<210>  2979
<211>  325
<212>  PRT
```

<213> Homo sapiens

<400> 2979

Met Pro Ile Thr Arg Met Arg Met Arg Pro Trp Leu Glu Met Gln Ile
1   5   10   15

Asn Ser Asn Gln Ile Pro Gly Leu Ile Trp Ile Asn Lys Glu Glu Met
            20   25   30

Ile Phe Gln Ile Pro Trp Lys His Ala Ala Lys His Gly Trp Asp Ile
        35   40   45

Asn Lys Asp Ala Cys Leu Phe Arg Ser Trp Ala Ile His Thr Gly Arg
    50   55   60

Tyr Lys Ala Gly Glu Lys Glu Pro Asp Pro Lys Thr Trp Lys Ala Asn
65   70   75   80

Phe Arg Cys Ala Met Asn Ser Leu Pro Asp Ile Glu Glu Val Lys Asp
                85   90   95

Gln Ser Arg Asn Lys Gly Ser Ser Ala Val Arg Val Tyr Arg Met Leu
            100   105   110

Pro Pro Leu Thr Lys Asn Gln Arg Lys Glu Arg Lys Ser Lys Ser Ser
        115   120   125

Arg Asp Ala Lys Ser Lys Ala Lys Arg Lys Ser Cys Gly Asp Ser Ser
    130   135   140

Pro Asp Thr Phe Ser Asp Gly Leu Ser Ser Ser Thr Leu Pro Asp Asp
145   150   155   160

His Ser Ser Tyr Thr Val Pro Gly Tyr Met Gln Asp Leu Glu Val Glu
                165   170   175

Gln Ala Leu Thr Pro Ala Leu Ser Pro Cys Ala Val Ser Ser Thr Leu
            180   185   190

Pro Asp Trp His Ile Pro Val Glu Val Val Pro Asp Ser Thr Ser Asp
        195   200   205

Leu Tyr Asn Phe Gln Val Ser Pro Met Pro Ser Thr Ser Glu Ala Thr
    210   215   220

Thr Asp Glu Asp Glu Glu Gly Lys Leu Pro Glu Asp Ile Met Lys Leu

225   230   235   240

Leu Glu Gln Ser Glu Trp Gln Pro Thr Asn Val Asp Gly Lys Gly Tyr
                245   250   255

Leu Leu Asn Glu Pro Gly Val Gln Pro Thr Ser Val Tyr Gly Asp Phe
                260   265   270

Ser Cys Lys Glu Glu Pro Glu Ile Asp Ser Pro Gly Gly Asp Ile Gly
            275   280   285

Leu Ser Leu Gln Arg Val Phe Thr Asp Leu Lys Asn Met Asp Ala Thr
    290   295   300

Trp Leu Asp Ser Leu Leu Thr Pro Val Arg Leu Pro Ser Ile Gln Ala
305   310   315   320

Ile Pro Cys Ala Pro
                325

<210> 2980
<211> 132
<212> PRT
<213> Homo sapiens

<400> 2980

Met Glu Phe Asp Leu Asn Gly Asn Gly Asp Ile Gly Glu Lys Arg Val
1   5   10   15

Ile Cys Gly Gly Arg Val Val Cys Arg Pro Lys Lys Thr Glu Val Ser
                20   25   30

Pro Thr Cys Ser Ile Pro His Asp Leu Gly Gly Gly Pro Pro Thr Thr
            35   40   45

Val Gly Gly Arg Arg Met Gly Met Arg Lys Trp Glu Arg Arg Glu Arg
    50   55   60

Val Ser Pro Pro Ser Pro His Pro His Pro Leu Pro Pro Asp Ile Met
65   70   75   80

Ser Leu Lys Arg Met Leu Glu Lys Leu Gly Val Pro Lys Thr His Leu
                85   90   95

Glu Leu Lys Lys Leu Ile Gly Glu Val Ser Ser Gly Ser Gly Glu Thr
                100   105   110

```
Phe Ser Tyr Pro Asp Phe Leu Arg Met Met Leu Gly Lys Arg Ser Ala
        115                 120                 125


Ile Leu Lys Met
    130
```

```
<210>   2981
<211>   319
<212>   PRT
<213>   Homo sapiens

<400>   2981
```

```
Met Thr Asn Ser Ser Phe Phe Cys Pro Val Tyr Lys Asp Leu Glu Pro
1               5                   10                  15


Phe Thr Tyr Phe Phe Tyr Leu Val Phe Leu Val Gly Ile Ile Gly Ser
        20                  25                  30


Cys Phe Ala Thr Trp Ala Phe Ile Gln Lys Asn Thr Asn His Arg Cys
        35                  40                  45


Val Ser Ile Tyr Leu Ile Asn Leu Leu Thr Ala Asp Phe Leu Leu Thr
    50                  55                  60


Leu Ala Leu Pro Val Lys Ile Val Val Asp Leu Gly Val Ala Pro Trp
65                  70                  75                  80


Lys Leu Lys Ile Phe His Cys Gln Val Thr Ala Cys Leu Ile Tyr Ile
                85                  90                  95


Asn Met Tyr Leu Ser Ile Ile Phe Leu Ala Phe Val Ser Ile Asp Arg
            100                 105                 110


Cys Leu Gln Leu Thr His Ser Cys Lys Ile Tyr Arg Ile Gln Glu Pro
        115                 120                 125


Gly Phe Ala Lys Met Ile Ser Thr Val Val Trp Leu Met Val Leu Leu
        130                 135                 140


Ile Met Val Pro Asn Met Met Ile Pro Ile Lys Asp Ile Lys Glu Lys
145                 150                 155                 160


Ser Asn Val Gly Cys Met Glu Phe Lys Lys Glu Phe Gly Arg Asn Trp
                165                 170                 175


His Leu Leu Thr Asn Phe Ile Cys Val Ala Ile Phe Leu Asn Phe Ser
```

                    180   185   190

    Ala Ile Ile Leu Ile Ser Asn Cys Leu Val Ile Arg Gln Leu Tyr Arg
            195   200   205

    Asn Lys Asp Asn Glu Asn Tyr Pro Asn Val Lys Lys Ala Leu Ile Asn
            210   215   220

    Ile Leu Leu Val Thr Thr Gly Tyr Ile Ile Cys Phe Val Pro Tyr His
    225   230   235   240

    Ile Val Arg Ile Pro Tyr Thr Leu Ser Gln Thr Glu Val Ile Thr Asp
                245   250   255

    Cys Ser Thr Arg Ile Ser Leu Phe Lys Ala Lys Glu Ala Thr Leu Leu
                260   265   270

    Leu Ala Val Ser Asn Leu Cys Phe Asp Pro Ile Leu Tyr Tyr His Leu
                275   280   285

    Ser Lys Ala Phe Arg Ser Lys Val Thr Glu Thr Phe Ala Ser Pro Lys
            290   295   300

    Glu Thr Lys Ala Gln Lys Glu Lys Leu Arg Cys Glu Asn Asn Ala
    305   310   315

    <210> 2982
    <211> 334
    <212> PRT
    <213> Homo sapiens

    <400> 2982

    Met Leu Thr Lys Pro Leu Gln Gly Pro Pro Ala Pro Pro Gly Thr Pro
    1   5   10   15

    Thr Pro Pro Pro Gly Gly Lys Asp Arg Glu Ala Phe Glu Ala Glu Tyr
                20   25   30

    Arg Leu Gly Pro Leu Leu Gly Lys Gly Gly Phe Gly Thr Val Phe Ala
            35   40   45

    Gly His Arg Leu Thr Asp Arg Leu Gln Val Ala Ile Lys Val Ile Pro
    50   55   60

    Arg Asn Arg Val Leu Gly Trp Ser Pro Leu Ser Asp Ser Val Thr Cys
    65   70   75   80

                                    1383

Pro Leu Glu Val Ala Leu Leu Trp Lys Val Gly Ala Gly Gly His
              85   90   95

Pro Gly Val Ile Arg Leu Leu Asp Trp Phe Glu Thr Gln Glu Gly Phe
              100   105   110

Met Leu Val Leu Glu Arg Pro Leu Pro Ala Gln Asp Leu Phe Asp Tyr
              115   120   125

Ile Thr Glu Lys Gly Pro Leu Gly Glu Gly Pro Ser Arg Cys Phe Phe
              130   135   140

Gly Gln Val Val Ala Ala Ile Gln His Cys His Ser Arg Gly Val Val
145   150   155   160

His Arg Asp Ile Lys Asp Glu Asn Ile Leu Ile Asp Leu Arg Arg Gly
              165   170   175

Cys Ala Lys Leu Ile Asp Phe Gly Ser Gly Ala Leu Leu His Asp Glu
              180   185   190

Pro Tyr Thr Asp Phe Asp Gly Thr Arg Val Tyr Ser Pro Pro Glu Trp
              195   200   205

Ile Ser Arg His Gln Tyr His Ala Leu Pro Ala Thr Val Trp Ser Leu
210   215   220

Gly Ile Leu Leu Tyr Asp Met Val Cys Gly Asp Ile Pro Phe Glu Arg
225   230   235   240

Asp Gln Glu Ile Leu Glu Ala Glu Leu His Phe Pro Ala His Val Ser
              245   250   255

Pro Asp Cys Cys Ala Leu Ile Arg Arg Cys Leu Ala Pro Lys Pro Ser
              260   265   270

Ser Arg Pro Ser Leu Glu Glu Ile Leu Leu Asp Pro Trp Met Gln Thr
              275   280   285

Pro Ala Glu Asp Val Thr Pro Gln Pro Leu Gln Arg Arg Pro Cys Pro
              290   295   300

Phe Gly Leu Val Leu Ala Thr Leu Ser Leu Ala Trp Pro Gly Leu Ala
305   310   315   320

```
Pro Asn Gly Gln Lys Ser His Pro Met Ala Met Ser Gln Gly
                325             330
```

```
<210>   2983
<211>   158
<212>   PRT
<213>   Homo sapiens

<400>   2983
```

```
Met Met Gln Lys Leu Leu Lys Cys Ser Arg Leu Val Leu Ala Leu Ala
1               5               10              15
```

```
Leu Ile Leu Val Leu Glu Ser Ser Val Gln Gly Tyr Pro Thr Gln Arg
            20              25              30
```

```
Ala Arg Tyr Gln Trp Val Arg Cys Asn Pro Asp Ser Asn Ser Ala Asn
        35              40              45
```

```
Cys Leu Glu Glu Lys Gly Pro Met Phe Glu Leu Leu Pro Gly Glu Ser
    50              55              60
```

```
Asn Lys Ile Pro Arg Leu Arg Thr Asp Leu Phe Pro Lys Thr Arg Ile
65              70              75              80
```

```
Gln Asp Leu Asn Arg Ile Phe Pro Leu Ser Glu Asp Tyr Ser Gly Ser
                85              90              95
```

```
Gly Phe Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Phe
            100             105             110
```

```
Leu Thr Glu Met Glu Gln Asp Tyr Gln Leu Val Asp Glu Ser Asp Ala
        115             120             125
```

```
Phe His Asp Asn Leu Arg Ser Leu Asp Arg Asn Leu Pro Ser Asp Ser
    130             135             140
```

```
Gln Asp Leu Gly Gln His Gly Leu Glu Glu Asp Phe Met Leu
145             150             155
```

```
<210>   2984
<211>   1019
<212>   PRT
<213>   Homo sapiens

<400>   2984
```

```
Ala Asp Pro Glu Ser Pro Ile Leu Asp Leu Asp Leu His Leu Pro Leu
1               5               10              15
```

```
Leu Cys Phe Arg Pro Glu Lys Val Leu Gln Ile Leu Thr Cys Ile Leu
         20                  25                  30


Thr Glu Gln Arg Ile Val Phe Phe Ser Ser Asp Trp Ala Leu Leu Thr
         35                  40                  45


Leu Val Thr Glu Cys Phe Met Ala Tyr Leu Tyr Pro Leu Gln Trp Gln
         50                  55                  60


His Pro Phe Val Pro Ile Leu Ser Asp Gln Met Leu Asp Phe Val Met
65                  70                  75                  80


Ala Pro Thr Ser Phe Leu Met Gly Cys His Leu Asp His Phe Glu Glu
                 85                  90                  95


Val Ser Lys Glu Ala Asp Gly Leu Val Leu Ile Asn Ile Asp His Gly
             100                 105                 110


Ser Ile Thr Tyr Ser Lys Ser Thr Asp Asp Asn Val Asp Ile Pro Asp
         115                 120                 125


Val Pro Leu Leu Ala Ala Gln Thr Phe Ile Gln Arg Val Gln Ser Leu
         130                 135                 140


Gln Leu His His Glu Leu His Ala Ala His Leu Leu Ser Ser Thr Asp
145                 150                 155                 160


Leu Lys Glu Gly Arg Ala His Arg Arg Ser Trp Gln Gln Lys Leu Asn
                 165                 170                 175


Cys Gln Ile Gln Gln Thr Thr Leu Gln Leu Leu Val Ser Ile Phe Arg
             180                 185                 190


Asp Val Lys Asn His Leu Asn Tyr Glu His Arg Val Phe Asn Ser Glu
         195                 200                 205


Glu Phe Leu Lys Thr Arg Ala Pro Gly Asp His Gln Phe Tyr Lys Gln
         210                 215                 220


Val Leu Asp Thr Tyr Met Phe His Ser Phe Leu Lys Ala Arg Leu Asn
225                 230                 235                 240


Arg Arg Met Asp Ala Phe Ala Gln Met Asp Leu Asp Thr Gln Ser Glu
                 245                 250                 255
```

```
Glu Asp Arg Ile Asn Gly Met Leu Leu Ser Pro Arg Arg Pro Thr Val
            260             265             270

Glu Lys Arg Ala Ser Arg Lys Ser Ser His Leu His Val Thr His Arg
            275             280             285

Arg Met Val Val Ser Met Pro Asn Leu Gln Asp Ile Ala Met Pro Glu
    290             295             300

Leu Ala Pro Arg Asn Ser Ser Leu Arg Leu Thr Asp Thr Ala Gly Cys
305             310             315             320

Arg Gly Ser Ser Ala Val Leu Asn Val Thr Pro Lys Ser Pro Tyr Thr
            325             330             335

Phe Lys Ile Pro Glu Ile His Phe Pro Leu Glu Ser Lys Cys Val Gln
            340             345             350

Ala Tyr His Ala His Phe Val Ser Met Leu Ser Glu Ala Met Cys Phe
            355             360             365

Leu Ala Pro Asp Asn Ser Leu Leu Leu Ala Arg Tyr Leu Tyr Leu Arg
    370             375             380

Gly Leu Val Tyr Leu Met Gln Gly Gln Leu Leu Asn Ala Leu Leu Asp
385             390             395             400

Phe Gln Asn Leu Tyr Lys Thr Asp Ile Arg Ile Phe Pro Thr Asp Leu
            405             410             415

Val Lys Arg Thr Val Glu Ser Met Ser Ala Pro Glu Trp Glu Gly Ala
            420             425             430

Glu Gln Ala Pro Glu Leu Met Arg Leu Ile Ser Glu Ile Leu Asp Lys
            435             440             445

Pro His Glu Ala Ser Lys Leu Asp Asp His Val Lys Lys Phe Lys Leu
    450             455             460

Pro Lys Lys His Met Gln Leu Gly Asp Phe Met Lys Arg Val Gln Glu
465             470             475             480

Ser Gly Ile Val Lys Asp Ala Ser Ile Ile His Arg Leu Phe Glu Ala
            485             490             495

Leu Thr Val Gly Gln Glu Lys Gln Ile Asp Pro Glu Thr Phe Lys Asp
```

                          500   505   510

      Phe Tyr Asn Cys Trp Lys Glu Thr Glu Ala Glu Ala Gln Glu Val Ser
                  515   520   525

      Leu Pro Trp Leu Val Met Glu His Leu Asp Lys Asn Glu Cys Val Cys
                  530   535   540

      Lys Leu Ser Ser Ser Val Lys Thr Asn Leu Gly Val Gly Lys Ile Ala
      545   550   555   560

      Met Thr Gln Lys Arg Leu Phe Leu Leu Thr Glu Gly Arg Pro Gly Tyr
                      565   570   575

      Leu Glu Ile Ser Thr Phe Arg Asn Ile Glu Glu Val Arg Arg Thr Thr
                      580   585   590

      Thr Thr Phe Leu Leu Arg Arg Ile Pro Thr Leu Lys Ile Arg Val Ala
                  595   600   605

      Ser Lys Lys Glu Val Phe Glu Ala Asn Leu Lys Thr Glu Cys Asp Leu
          610   615   620

      Trp His Leu Met Val Lys Glu Met Trp Ala Gly Lys Lys Leu Ala Asp
      625   630   635   640

      Asp His Lys Asp Pro His Tyr Val Gln Gln Ala Leu Thr Asn Val Leu
                      645   650   655

      Leu Met Asp Ala Val Val Gly Thr Leu Gln Ser Pro Gly Ala Ile Tyr
                  660   665   670

      Ala Ala Ser Lys Leu Ser Tyr Phe Asp Lys Met Ser Asn Glu Met Pro
          675   680   685

      Met Thr Leu Pro Glu Thr Thr Leu Glu Thr Leu Lys His Lys Ile Asn
          690   695   700

      Pro Ser Ala Gly Glu Ala Phe Pro Gln Ala Val Asp Val Leu Leu Tyr
      705   710   715   720

      Thr Pro Gly His Leu Asp Pro Ala Glu Lys Val Glu Asp Ala His Pro
                      725   730   735

      Lys Leu Trp Cys Ala Leu Ser Glu Gly Lys Val Thr Val Phe Asn Ala
                  740   745   750

                                      1388

```
Ser Ser Trp Thr Ile His Gln His Ser Phe Lys Val Gly Thr Ala Lys
        755                 760             765

Val Asn Cys Met Val Met Ala Asp Gln Asn Gln Val Trp Val Gly Ser
    770             775                 780

Glu Asp Ser Val Ile Tyr Ile Ile Asn Val His Ser Met Ser Cys Asn
785             790                 795                     800

Lys Gln Leu Thr Ala His Cys Ser Ser Val Thr Asp Leu Ile Val Gln
                805                 810                 815

Asp Gly Gln Glu Ala Pro Ser Asn Val Tyr Ser Cys Ser Met Asp Gly
            820                 825                 830

Met Val Leu Val Trp Asn Val Ser Thr Leu Gln Val Thr Ser Arg Phe
        835                 840                 845

Gln Leu Pro Arg Gly Gly Leu Thr Ser Ile Arg Leu His Gly Gly Arg
    850                 855                 860

Leu Trp Cys Cys Thr Gly Asn Ser Ile Met Val Met Lys Met Asn Gly
865                 870                 875                 880

Ser Leu His Gln Glu Leu Lys Ile Glu Glu Asn Phe Lys Asp Thr Ser
            885                 890                 895

Thr Ser Phe Leu Ala Phe Gln Leu Leu Pro Glu Glu Glu Gln Leu Trp
            900                 905             ·   910

Ala Ala Cys Ala Gly Arg Ser Glu Val Tyr Ile Trp Ser Leu Lys Asp
        915                 920                 925

Leu Ala Gln Pro Pro Gln Arg Val Pro Leu Glu Asp Cys Ser Glu Ile
    930                 935                 940

Asn Cys Met Ile Arg Val Lys Lys Gln Val Trp Val Gly Ser Arg Gly
945                 950                 955                 960

Leu Gly Gln Gly Thr Pro Lys Gly Lys Ile Tyr Val Ile Asp Ala Glu
                965                 970                 975
·

Arg Lys Thr Val Glu Lys Glu Leu Val Ala His Met Asp Thr Val Arg
            980                 985                 990
```

Thr Leu Cys Ser Ala Glu Asp Arg Tyr Val Leu Ser Gly Ser Gly Arg
        995   1000   1005

Glu Glu Gly Lys Val Ala Ile Trp Lys Gly Glu
    1010   1015

<210> 2985
<211> 783
<212> PRT
<213> Homo sapiens

<400> 2985

Met Ala Lys Tyr Asn Thr Gly Gly Asn Pro Thr Glu Asp Val Ser Val
1   5   10   15

Asn Ser Arg Pro Phe Arg Val Thr Gly Pro Asn Ser Ser Ser Gly Ile
            20   25   30

Gln Ala Arg Lys Asn Leu Phe Asn Asn Gln Gly Asn Ala Ser Pro Pro
        35   40   45

Ala Gly Pro Ser Asn Val Pro Lys Phe Gly Ser Pro Lys Pro Pro Val
    50   55   60

Ala Val Lys Pro Ser Ser Glu Glu Lys Pro Asp Lys Glu Pro Lys Pro
65   70   75   80

Pro Phe Leu Lys Pro Thr Gly Ala Gly Gln Arg Phe Gly Thr Pro Ala
            85   90   95

Ser Leu Thr Thr Arg Asp Pro Glu Ala Lys Val Gly Phe Leu Lys Pro
        100   105   110

Val Gly Pro Lys Pro Ile Asn Leu Pro Lys Glu Asp Ser Lys Pro Thr
        115   120   125

Phe Pro Trp Pro Pro Gly Asn Lys Pro Ser Leu His Ser Val Asn Gln
    130   135   140

Asp His Asp Leu Lys Pro Leu Gly Pro Lys Ser Gly Pro Thr Pro Pro
145   150   155   160

Thr Ser Glu Asn Glu Gln Lys Gln Ala Phe Pro Lys Leu Thr Gly Val
            165   170   175

Lys Gly Lys Phe Met Ser Ala Ser Gln Asp Leu Glu Pro Lys Pro Leu

                    180   . 185   190

Phe Pro Lys Pro Ala Phe Gly Gln Lys Pro Pro Leu Ser Thr Glu Asn
        195   200   205

Ser His Glu Asp Glu Ser Pro Met Lys Asn Val Ser Ser Ser Lys Gly
    210   215   220

Ser Pro Ala Pro Leu Gly Val Arg Ser Lys Ser Gly Pro Leu Lys Pro
225   230   235   240

Ala Arg Glu Asp Ser Glu Asn Lys Asp His Ala Gly Glu Ile Ser Ser
            245   250   255

Leu Pro Phe Pro Gly Val Val Leu Lys Pro Ala Ala Ser Arg Gly Gly
        260   265   270

Leu Gly Leu Ser Lys Asn Gly Glu Glu Lys Lys Glu Asp Arg Lys Ile
        275   280   285

Asp Ala Ala Lys Asn Thr Phe Gln Ser Lys Ile Asn Gln Glu Glu Leu
    290   295   300

Ala Ser Gly Thr Pro Pro Ala Arg Phe Pro Lys Ala Pro Ser Lys Leu
305   310   315   320

Thr Val Gly Gly Pro Trp Gly Gln Ser Gln Glu Lys Glu Lys Gly Asp
            325   330   335

Lys Asn Ser Ala Thr Pro Lys Gln Lys Pro Leu Pro Pro Leu Phe Thr
            340   345   350

Leu Gly Pro Pro Pro Lys Pro Asn Arg Pro Pro Asn Val Asp Leu
        355   360   365

Thr Lys Phe His Lys Thr Ser Ser Gly Asn Ser Thr Ser Lys Gly Gln
    370   375   380

Thr Ser Tyr Ser Thr Thr Ser Leu Pro Pro Pro Pro Ser His Pro
385   390   395   400

Ala Ser Gln Pro Pro Leu Pro Ala Ser His Pro Ser Gln Pro Pro Val
            405   410   415

Pro Ser Leu Pro Pro Arg Asn Ile Lys Pro Pro Phe Asp Leu Lys Ser
            420   425   430

Pro Val Asn Glu Asp Asn Gln Asp Gly Val Thr His Ser Asp Gly Ala
        435   440   445

Gly Asn Leu Asp Glu Glu Gln Asp Ser Glu Gly Glu Thr Tyr Glu Asp
        450   455   460

Ile Glu Ala Ser Lys Glu Arg Glu Lys Lys Arg Glu Lys Glu Glu Lys
465   470   475   480

Lys Arg Leu Glu Leu Glu Lys Lys Glu Gln Lys Glu Lys Glu Lys Lys
                485   490   495

Glu Gln Glu Ile Lys Lys Lys Phe Lys Leu Thr Gly Pro Ile Gln Val
                500   505   510

Ile His Leu Ala Lys Ala Cys Cys Asp Val Lys Gly Gly Lys Asn Glu
        515   520   525

Leu Ser Phe Lys Gln Gly Glu Gln Ile Glu Ile Ile Arg Ile Thr Asp
        530   535   540

Asn Pro Glu Gly Lys Trp Leu Gly Arg Thr Ala Arg Gly Ser Tyr Gly
545   550   555   560

Tyr Ile Lys Thr Thr Ala Val Glu Ile Asp Tyr Asp Ser Leu Lys Leu
                565   570   575

Lys Lys Asp Ser Leu Gly Ala Pro Ser Arg Pro Ile Glu Asp Asp Gln
                580   585   590

Glu Val Tyr Asp Asp Val Ala Glu Gln Asp Asp Ile Ser Ser His Ser
        595   600   605

Gln Ser Gly Ser Gly Gly Ile Phe Pro Pro Pro Asp Asp Asp Ile
        610   615   620

Tyr Asp Gly Ile Glu Glu Glu Asp Ala Asp Asp Gly Phe Pro Ala Pro
625   630   635   640

Pro Lys Gln Leu Asp Met Gly Asp Glu Val Tyr Asp Asp Val Asp Thr
                645   650   655

Ser Asp Phe Pro Val Ser Ser Ala Glu Met Ser Gln Gly Thr Asn Phe
        660   665   670

1392

```
Gly Lys Ala Lys Thr Glu Glu Lys Asp Leu Lys Lys Leu Lys Lys Gln
        675                 680                 685

Glu Lys Glu Glu Lys Asp Phe Arg Lys Lys Phe Lys Tyr Asp Gly Glu
        690                 695                 700

Ile Arg Val Leu Tyr Ser Thr Lys Val Thr Thr Ser Ile Thr Ser Lys
705                 710                 715                 720

Lys Trp Gly Thr Arg Asp Leu Gln Val Lys Pro Gly Glu Ser Leu Glu
                725                 730                 735

Val Ile Gln Thr Thr Asp Asp Thr Lys Val Leu Cys Arg Asn Glu Glu
            740                 745                 750

Gly Lys Tyr Gly Tyr Val Leu Arg Ser Tyr Leu Ala Asp Asn Asp Gly
        755                 760                 765

Glu Ile Tyr Asp Asp Ile Ala Asp Gly Cys Ile Tyr Asp Asn Asp
    770                 775                 780
```

```
<210>  2986
<211>  266
<212>  PRT
<213>  Homo sapiens

<400>  2986
```

```
Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1               5                   10                  15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
            20                  25                  30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
        35                  40                  45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
    50                  55                  60

Glu Phe Leu Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65                  70                  75                  80

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Leu
                85                  90                  95

Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
```

                100   105   110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
        115   120   125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
    130   135   140

Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145   150   155   160

Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu
            165   170   175

Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr
        180   185   190

Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
    195   200   205

Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala
    210   215   220

Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu
225   230   235   240

Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
            245   250   255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
            260   265

<210>   2987
<211>   363
<212>   PRT
<213>   Homo sapiens

<400>   2987

Met Glu Val Lys Lys Lys Lys His Asp Lys Gln Glu Gln Lys Gly Ser
1   5   10   15

Val Gly Ala Thr Phe Lys Leu Gly Asp Ser Leu Ser Asn Pro Asn Glu
            20   25   30

Arg Ala Ile Val Lys Glu Lys Met Val Ser Asn Thr Lys Ser Val Asp
        35   40   45

Thr Lys Ala Ser Ser Ser Lys Phe Ser Arg Ile Leu Thr Pro Lys Glu
    50   55   60

Tyr Leu Gln Arg Gln Lys His Lys Glu Ala Pro Ser Asn Lys Ala Ser
65   70   75   80

Lys Lys Ile Cys Val Lys Asn Val Pro Cys Asp Ser Glu His Met Arg
                85   90   95

Pro Ser Lys Leu Ala Val Gln Val Glu Ser Cys Gly Lys Ser Asn Glu
                100   105   110

Lys His Ser Ser Gly Val Gln Thr Ser Lys Glu Ser Leu Asn Gly Leu
            115   120   125

Thr Ser His Gly Lys Asn Leu Lys Ile His His Ser Gln Glu Ser Lys
    130   135   140

Thr Tyr Asn Ile Leu Arg Asn Val Lys Glu Lys Val Gly Gly Lys Gln
145   150   155   160

Pro Asp Lys Ile Trp Ile Asp Lys Thr Lys Leu Asp Lys Leu Thr Asn
            165   170   175

Ile Ser Asn Glu Ala Gln Phe Ser Gln Met Pro Pro Gln Val Lys Asp
            180   185   190

Gln Lys Lys Leu Tyr Leu Asn Arg Val Gly Phe Lys Cys Thr Glu Arg
        195   200   205

Glu Ser Ile Ser Leu Thr Lys Leu Glu Ser Ser Pro Arg Lys Leu His
    210   215   220

Lys Asp Lys Arg Gln Glu Asn Lys His Lys Thr Phe Leu Pro Val Lys
225   230   235   240

Gly Asn Thr Glu Lys Ser Asn Met Leu Glu Phe Lys Leu Cys Pro Asp
                245   250   255

Ile Leu Leu Lys Asn Thr Asn Ser Val Glu Glu Arg Lys Asp Val Lys
            260   265   270

Pro His Pro Arg Lys Glu Gln Ala Pro Leu Gln Val Ser Gly Ile Lys
    275   280   285

1395

```
Ser Thr Lys Glu Asp Trp Leu Lys Phe Val Ala Thr Lys Lys Arg Thr
    290                 295             300

Gln Lys Asp Ser Gln Glu Arg Asp Asn Val Asn Ser Arg Leu Ser Lys
305             310                 315                 320

Arg Ser Phe Ser Ala Asp Gly Phe Glu Met Leu Gln Asn Pro Val Lys
            325                 330                 335

Asp Ser Lys Glu Met Phe Gln Thr Tyr Lys Gln Met Tyr Leu Glu Lys
        340                 345                 350

Arg Ser Arg Ser Leu Gly Ser Ser Pro Val Lys
        355                 360
```

<210> 2988
<211> 836
<212> PRT
<213> Homo sapiens

<400> 2988

```
Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1               5                   10                  15

Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
            20                  25                  30

Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
        35                  40                  45

Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
    50                  55                  60

Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp
65                  70                  75                  80

Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
                85                  90                  95

Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
            100                 105                 110

Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn
        115                 120                 125

Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
130                 135                 140
```

1396

```
Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145             150             155             160

Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
                165             170             175

Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
            180             185             190

Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
        195             200             205

Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
    210             215             220

Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225             230             235             240

Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
                245             250             255

Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro
            260             265             270

Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu
        275             280             285

Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr
    290             295             300

Leu Gln Ile Arg Cys Ile Arg Trp Pro Leu Pro Gly His Trp Ser Asp
305             310             315             320

Trp Ser Pro Ser Leu Glu Leu Arg Thr Thr Glu Arg Ala Pro Thr Val
                325             330             335

Arg Leu Asp Thr Trp Trp Arg Gln Arg Gln Leu Asp Pro Arg Thr Val
            340             345             350

Gln Leu Phe Trp Lys Pro Val Pro Leu Glu Glu Asp Ser Gly Arg Ile
        355             360             365

Gln Gly Tyr Val Val Ser Trp Arg Pro Ser Gly Gln Ala Gly Ala Ile
    370             375             380
```

```
Leu Pro Leu Cys Asn Thr Thr Glu Leu Ser Cys Thr Phe His Leu Pro
385             390             395             400


Ser Glu Ala Gln Glu Val Ala Leu Val Ala Tyr Asn Ser Ala Gly Thr
                405             410             415


Ser Arg Pro Thr Pro Val Val Phe Ser Glu Ser Arg Gly Pro Ala Leu
            420             425             430


Thr Arg Leu His Ala Met Ala Arg Asp Pro His Ser Leu Trp Val Gly
        435             440             445


Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile Glu Trp Gly
    450             455             460


Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp Arg Met Glu
465             470             475             480


Gln Asn Gly Arg Ala Thr Gly Phe Leu Leu Lys Glu Asn Ile Arg Pro
            485             490             495


Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
            500             505             510


Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
        515             520             525


His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln
    530             535             540


Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
545             550             555             560


His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
            565             570             575


Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
            580             585             590


Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
        595             600             605


Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
610             615             620
```

```
Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr
625                 630             635                     640

Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
            645             650                     655

Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
            660             665                 670

Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu
            675             680                 685

Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys
    690             695             700

Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu
705             710             715                     720

Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val
            725             730                 735

Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr
            740             745                 750

Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu
    755             760             765

Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro
    770             775             780

Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu
785             790             795                     800

Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu
            805             810                 815

Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val His Gly Met Glu Ala
            820             825             830

Leu Gly Ser Phe
        835
```

<210> 2989
<211> 276
<212> PRT
<213> Homo sapiens

<400> 2989

Met Gly Asn Ser Met Lys Ser Thr Pro Ala Pro Ala Glu Arg Pro Leu
1   5   10   15

Pro Asn Pro Glu Gly Leu Asp Ser Asp Phe Leu Ala Val Leu Ser Asp
            20   25   30

Tyr Pro Ser Pro Asp Ile Ser Pro Pro Ile Phe Arg Arg Gly Glu Lys
        35   40   45

Leu Arg Val Ile Ser Asp Glu Gly Gly Trp Trp Lys Ala Ile Ser Leu
    50   55   60

Ser Thr Gly Arg Glu Ser Tyr Ile Pro Gly Ile Cys Val Ala Arg Val
65   70   75   80

Tyr His Gly Trp Leu Phe Glu Gly Leu Gly Arg Asp Lys Ala Glu Glu
            85   90   95

Leu Leu Gln Leu Pro Asp Thr Lys Val Gly Ser Phe Met Ile Arg Glu
        100   105   110

Ser Glu Thr Lys Lys Gly Phe Tyr Ser Leu Ser Val Arg His Arg Gln
        115   120   125

Val Lys His Tyr Arg Ile Phe Arg Leu Pro Asn Asn Trp Tyr Tyr Ile
    130   135   140

Ser Pro Arg Leu Thr Phe Gln Cys Leu Glu Asp Leu Val Asn His Tyr
145   150   155   160

Ser Glu Val Ala Asp Gly Leu Cys Cys Val Leu Thr Thr Pro Cys Leu
            165   170   175

Thr Gln Ser Thr Ala Ala Pro Ala Val Arg Ala Ser Ser Ser Pro Val
            180   185   190

Thr Leu Arg Gln Lys Thr Val Asp Trp Arg Arg Val Ser Arg Leu Gln
        195   200   205

Glu Asp Pro Glu Gly Thr Glu Asn Pro Leu Gly Val Asp Glu Ser Leu
    210   215   220

Phe Ser Tyr Gly Leu Arg Glu Ser Ile Ala Ser Tyr Leu Ser Leu Thr
225   230   235   240

Ser Glu Asp Asn Thr Ser Phe Asp Arg Lys Lys Lys Ser Ile Ser Leu
            245   250   255

Met Tyr Gly Gly Ser Lys Arg Lys Ser Ser Phe Phe Ser Ser Pro Pro
            260   265   270

Tyr Phe Glu Asp
        275

<210> 2990
<211> 359
<212> PRT
<213> Homo sapiens

<400> 2990

Met Ala Pro Asn Gly Thr Ala Ser Ser Phe Cys Leu Asp Ser Thr Ala
1   5   10   15

Cys Lys Ile Thr Ile Thr Val Val Leu Ala Val Leu Ile Leu Ile Thr
            20   25   30

Val Ala Gly Asn Val Val Val Cys Leu Ala Val Gly Leu Asn Arg Arg
        35   40   45

Leu Arg Asn Leu Thr Asn Cys Phe Ile Val Ser Leu Ala Ile Thr Asp
    50   55   60

Leu Leu Leu Gly Leu Leu Val Leu Pro Phe Ser Ala Ile Tyr Gln Leu
65   70   75   80

Ser Cys Lys Trp Ser Phe Gly Lys Val Phe Cys Asn Ile Tyr Thr Ser
            85   90   95

Leu Asp Val Met Leu Cys Thr Ala Ser Ile Leu Asn Leu Phe Met Ile
            100   105   110

Ser Leu Asp Arg Tyr Cys Ala Val Met Asp Pro Leu Arg Tyr Pro Val
            115   120   125

Leu Val Thr Pro Val Arg Val Ala Ile Ser Leu Val Leu Ile Trp Val
            130   135   140

Ile Ser Ile Thr Leu Ser Phe Leu Ser Ile His Leu Gly Trp Asn Ser
145   150   155   160

Arg Asn Glu Thr Ser Lys Gly Asn His Thr Thr Ser Lys Cys Lys Val

```
                  165                    170                    175
```

Gln Val Asn Glu Val Tyr Gly Leu Val Asp Gly Leu Val Thr Phe Tyr
              180   185   190

Leu Pro Leu Leu Ile Met Cys Ile Thr Tyr Tyr Arg Ile Phe Lys Val
          195   200   205

Ala Arg Asp Gln Ala Lys Arg Ile Asn His Ile Ser Ser Trp Lys Ala
      210   215   220

Ala Thr Ile Arg Glu His Lys Ala Thr Val Thr Leu Ala Ala Val Met
225   230   235   240

Gly Ala Phe Ile Ile Cys Trp Phe Pro Tyr Phe Thr Ala Phe Val Tyr
              245   250   255

Arg Gly Leu Arg Gly Asp Asp Ala Ile Asn Glu Val Leu Glu Ala Ile
          260   265   270

Val Leu Trp Leu Gly Tyr Ala Asn Ser Ala Leu Asn Pro Ile Leu Tyr
      275   280   285

Ala Ala Leu Asn Arg Asp Phe Arg Thr Gly Tyr Gln Gln Leu Phe Cys
      290   295   300

Cys Arg Leu Ala Asn Arg Asn Ser His Lys Thr Ser Leu Arg Ser Asn
305   310   315   320

Ala Ser Gln Leu Ser Arg Thr Gln Ser Arg Glu Pro Arg Gln Gln Glu
              325   330   335

Glu Lys Pro Leu Lys Leu Gln Val Trp Ser Gly Thr Glu Val Thr Ala
          340   345   350

Pro Gln Gly Ala Thr Asp Arg
          355

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<210>   2991
<211>   505
<212>   PRT
<213>   Homo sapiens

<400>   2991
```

Met Gly Ser Met Lys Ser Lys Phe Leu Gln Val Gly Gly Asn Thr Phe
1   5   10   15

Ser Lys Thr Glu Thr Ser Ala Ser Pro His Cys Pro Val Tyr Val Pro
        20   25   30

Asp Pro Thr Ser Thr Ile Lys Pro Gly Pro Asn Ser His Asn Ser Asn
        35   40   45

Thr Pro Gly Ile Arg Glu Ala Gly Ser Glu Asp Ile Ile Val Val Ala
        50   55   60

Leu Tyr Asp Tyr Glu Ala Ile His His Glu Asp Leu Ser Phe Gln Lys
65   70   75   80

Gly Asp Gln Met Val Val Leu Glu Glu Ser Gly Glu Trp Trp Lys Ala
                85   90   95

Arg Ser Leu Ala Thr Arg Lys Glu Gly Tyr Ile Pro Ser Asn Tyr Val
            100   105   110

Ala Arg Val Asp Ser Leu Glu Thr Glu Glu Trp Phe Phe Lys Gly Ile
            115   120   125

Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro Gly Asn Met Leu
    130   135   140

Gly Ser Phe Met Ile Arg Asp Ser Glu Thr Thr Lys Gly Ser Tyr Ser
145   150   155   160

Leu Ser Val Arg Asp Tyr Asp Pro Arg Gln Gly Asp Thr Val Lys His
            165   170   175

Tyr Lys Ile Arg Thr Leu Asp Asn Gly Gly Phe Tyr Ile Ser Pro Arg
            180   185   190

Ser Thr Phe Ser Thr Leu Gln Glu Leu Val Asp His Tyr Lys Lys Gly
        195   200   205

Asn Asp Gly Leu Cys Gln Lys Leu Ser Val Pro Cys Met Ser Ser Lys
    210   215   220

Pro Gln Lys Pro Trp Glu Lys Asp Ala Trp Glu Ile Pro Arg Glu Ser
225   230   235   240

Leu Lys Leu Glu Lys Lys Leu Gly Ala Gly Gln Phe Gly Glu Val Trp
            245   250   255

Met Ala Thr Tyr Asn Lys His Thr Lys Val Ala Val Lys Thr Met Lys
        260   265   270

Pro Gly Ser Met Ser Val Glu Ala Phe Leu Ala Glu Ala Asn Val Met
        275   280   285

Lys Thr Leu Gln His Asp Lys Leu Val Lys Leu His Ala Val Val Thr
        290   295   300

Lys Glu Pro Ile Tyr Ile Ile Thr Glu Phe Met Ala Lys Gly Ser Leu
305   310   315   320

Leu Asp Phe Leu Lys Ser Asp Glu Gly Ser Lys Gln Pro Leu Pro Lys
            325   330   335

Leu Ile Asp Phe Ser Ala Gln Ile Ala Glu Gly Met Ala Phe Ile Glu
            340   345   350

Gln Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala Asn Ile Leu Val
        355   360   365

Ser Ala Ser Leu Val Cys Lys Ile Ala Asp Phe Gly Leu Ala Arg Val
        370   375   380

Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile
385   390   395   400

Lys Trp Thr Ala Pro Glu Ala Ile Asn Phe Gly Ser Phe Thr Ile Lys
            405   410   415

Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Met Glu Ile Val Thr Tyr
            420   425   430

Gly Arg Ile Pro Tyr Pro Gly Met Ser Asn Pro Glu Val Ile Arg Ala
        435   440   445

Leu Glu Arg Gly Tyr Arg Met Pro Arg Pro Glu Asn Cys Pro Glu Glu
        450   455   460

Leu Tyr Asn Ile Met Met Arg Cys Trp Lys Asn Arg Pro Glu Glu Arg
465   470   475   480

Pro Thr Phe Glu Tyr Ile Gln Ser Val Leu Asp Asp Phe Tyr Thr Ala
            485   490   495

Thr Glu Ser Gln Tyr Gln Gln Gln Pro

                        500   505

    <210>   2992
    <211>   1333
    <212>   PRT
    <213>   Homo sapiens

    <400>   2992

    Met Thr Ala Asp Lys Leu Val Phe Phe Val Asn Gly Arg Lys Val Val
    1   5   10   15

    Glu Lys Asn Ala Asp Pro Glu Thr Thr Leu Leu Ala Tyr Leu Arg Arg
                20   25   30

    Lys Leu Gly Leu Ser Gly Thr Lys Leu Gly Cys Gly Glu Gly Gly Cys
            35   40   45

    Gly Ala Cys Thr Val Met Leu Ser Lys Tyr Asp Arg Leu Gln Asn Lys
        50   55   60

    Ile Val His Phe Ser Ala Asn Ala Cys Leu Ala Pro Ile Cys Ser Leu
    65   70   75   80

    His His Val Ala Val Thr Thr Val Glu Gly Ile Gly Ser Thr Lys Thr
                85   90   95

    Arg Leu His Pro Val Gln Glu Arg Ile Ala Lys Ser His Gly Ser Gln
                100   105   110

    Cys Gly Phe Cys Thr Pro Gly Ile Val Met Ser Met Tyr Thr Leu Leu
            115   120   125

    Arg Asn Gln Pro Glu Pro Thr Met Glu Glu Ile Glu Asn Ala Phe Gln
        130   135   140

    Gly Asn Leu Cys Arg Cys Thr Gly Tyr Arg Pro Ile Leu Gln Gly Phe
    145   150   155   160

    Arg Thr Phe Ala Arg Asp Gly Gly Cys Cys Gly Gly Asp Gly Asn Asn
                165   170   175

    Pro Asn Cys Cys Met Asn Gln Lys Lys Asp His Ser Val Ser His Ser
                180   185   190

    Pro Ser Leu Phe Lys Pro Glu Glu Phe Thr Pro Leu Asp Pro Thr Gln
                195   200   205

Glu Pro Ile Phe Pro Pro Glu Leu Leu Arg Leu Lys Asp Thr Pro Arg
    210   215   220

Lys Gln Leu Arg Phe Glu Arg Glu Arg Val Thr Trp Ile Gln Ala Ser
225   230   235   240

Thr Leu Lys Glu Leu Leu Asp Leu Lys Ala Gln His Pro Asp Ala Lys
            245   250   255

Leu Val Val Gly Asn Thr Glu Ile Gly Ile Glu Met Lys Phe Lys Asn
            260   265   270

Met Leu Phe Pro Met Ile Val Cys Pro Ala Trp Ile Pro Glu Leu Asn
        275   280   285

Ser Val Glu His Gly Pro Asp Gly Ile Ser Phe Gly Ala Ala Cys Pro
    290   295   300

Leu Ser Ile Val Glu Lys Thr Leu Val Asp Ala Val Ala Lys Leu Pro
305   310   315   320

Ala Gln Lys Thr Glu Val Phe Arg Gly Val Leu Glu Gln Leu Arg Trp
            325   330   335

Phe Ala Gly Lys Gln Val Lys Ser Val Ala Ser Val Gly Gly Asn Ile
        340   345   350

Ile Thr Ala Ser Pro Ile Ser Asp Leu Asn Pro Val Phe Met Ala Ser
        355   360   365

Gly Ala Lys Leu Thr Leu Val Ser Arg Gly Thr Arg Arg Thr Val Gln
    370   375   380

Met Asp His Thr Phe Phe Pro Gly Tyr Arg Lys Thr Leu Leu Ser Pro
385   390   395   400

Glu Glu Ile Leu Leu Ser Ile Glu Ile Pro Tyr Ser Arg Glu Gly Glu
            405   410   415

Tyr Phe Ser Ala Phe Lys Gln Ala Ser Arg Arg Glu Asp Asp Ile Ala
        420   425   430

Lys Val Thr Ser Gly Met Arg Val Leu Phe Lys Pro Gly Thr Thr Glu
        435   440   445

```
Val Gln Glu Leu Ala Leu Cys Tyr Gly Gly Met Ala Asn Arg Thr Ile
    450             455             460

Ser Ala Leu Lys Thr Thr Gln Arg Gln Leu Ser Lys Leu Trp Lys Glu
465             470             475             480

Glu Leu Leu Gln Asp Val Cys Ala Gly Leu Ala Glu Glu Leu His Leu
            485             490             495

Pro Pro Asp Ala Pro Gly Gly Met Val Asp Phe Arg Cys Thr Leu Thr
            500             505             510

Leu Ser Phe Phe Phe Lys Phe Tyr Leu Thr Val Leu Gln Lys Leu Gly
            515             520             525

Gln Glu Asn Leu Glu Asp Lys Cys Gly Lys Leu Asp Pro Thr Phe Ala
    530             535             540

Ser Ala Thr Leu Leu Phe Gln Lys Asp Pro Pro Ala Asp Val Gln Leu
545             550             555             560

Phe Gln Glu Val Pro Lys Gly Gln Ser Glu Glu Asp Met Val Gly Arg
                565             570             575

Pro Leu Pro His Leu Ala Ala Asp Met Gln Ala Ser Gly Glu Ala Val
            580             585             590

Tyr Cys Asp Asp Ile Pro Arg Tyr Glu Asn Glu Leu Ser Leu Arg Leu
    595             600             605

Val Thr Ser Thr Arg Ala His Ala Lys Ile Lys Ser Ile Asp Thr Ser
    610             615             620

Glu Ala Lys Lys Val Pro Gly Phe Val Cys Phe Ile Ser Ala Asp Asp
625             630             635             640

Val Pro Gly Ser Asn Ile Thr Gly Ile Cys Asn Asp Glu Thr Val Phe
            645             650             655

Ala Lys Asp Lys Val Thr Cys Val Gly His Ile Ile Gly Ala Val Val
            660             665             670

Ala Asp Thr Pro Glu His Thr Gln Arg Ala Ala Gln Gly Val Lys Ile
            675             680             685

Thr Tyr Glu Glu Leu Pro Ala Ile Ile Thr Ile Glu Asp Ala Ile Lys
```

```
           690                    695                    700


Asn Asn Ser Phe Tyr Gly Pro Glu Leu Lys Ile Glu Lys Gly Asp Leu
705             710             715             720


Lys Lys Gly Phe Ser Glu Ala Asp Asn Val Val Ser Gly Glu Ile Tyr
                725             730             735


Ile Gly Gly Gln Glu His Phe Tyr Leu Glu Thr His Cys Thr Ile Ala
            740             745             750


Val Pro Lys Gly Glu Ala Gly Glu Met Glu Leu Phe Val Ser Thr Gln
            755             760             765


Asn Thr Met Lys Thr Gln Ser Phe Val Ala Lys Met Leu Gly Val Pro
    770             775             780


Ala Asn Arg Ile Val Val Arg Val Lys Arg Met Gly Gly Gly Phe Gly
785             790             795             800


Gly Lys Glu Thr Arg Ser Thr Val Val Ser Thr Ala Val Ala Leu Ala
            805             810             815


Ala Tyr Lys Thr Gly Arg Pro Val Arg Cys Met Leu Asp Arg Asp Glu
            820             825             830


Asp Met Leu Ile Thr Gly Gly Arg His Pro Phe Leu Ala Arg Tyr Lys
            835             840             845


Val Gly Phe Met Lys Thr Gly Thr Val Val Ala Leu Glu Val Asp His
            850             855             860


Phe Ser Asn Val Gly Asn Thr Gln Asp Leu Ser Gln Ser Ile Met Glu
865             870             875             880


Arg Ala Leu Phe His Met Asp Asn Cys Tyr Lys Ile Pro Asn Ile Arg
            885             890             895


Gly Thr Gly Arg Leu Cys Lys Thr Asn Leu Pro Ser Asn Thr Ala Phe
            900             905             910


Arg Gly Phe Gly Gly Pro Gln Gly Met Leu Ile Ala Glu Cys Trp Met
            915             920             925


Ser Glu Val Ala Val Thr Cys Gly Met Pro Ala Glu Glu Val Arg Arg
    930             935             940
```

Lys Asn Leu Tyr Lys Glu Gly Asp Leu Thr His Phe Asn Gln Lys Leu
945   950   955   960

Glu Gly Phe Thr Leu Pro Arg Cys Trp Glu Glu Cys Leu Ala Ser Ser
                965   970   975

Gln Tyr His Ala Arg Lys Ser Glu Val Asp Lys Phe Asn Lys Glu Asn
                980   985   990

Cys Trp Lys Lys Arg Gly Leu Cys Ile Ile Pro Thr Lys Phe Gly Ile
                995   1000   1005

Ser Phe Thr Val Pro Phe Leu Asn Gln Ala Gly Ala Leu Leu His
        1010   1015   1020

Val Tyr Thr Asp Gly Ser Val Leu Leu Thr His Gly Gly Thr Glu
        1025   1030   1035

Met Gly Gln Gly Leu His Thr Lys Met Val Gln Val Ala Ser Arg
        1040   1045   1050

Ala Leu Lys Ile Pro Thr Ser Lys Ile Tyr Ile Ser Glu Thr Ser
        1055   1060   1065

Thr Asn Thr Val Pro Asn Thr Ser Pro Thr Ala Ala Ser Val Ser
        1070   1075   1080

Ala Asp Leu Asn Gly Gln Ala Val Tyr Ala Ala Cys Gln Thr Ile
        1085   1090   1095

Leu Lys Arg Leu Glu Pro Tyr Lys Lys Lys Asn Pro Ser Gly Ser
        1100   1105   1110

Trp Glu Asp Trp Val Thr Ala Ala Tyr Met Asp Thr Val Ser Leu
        1115   1120   1125

Ser Ala Thr Gly Phe Tyr Arg Thr Pro Asn Leu Gly Tyr Ser Phe
        1130   1135   1140

Glu Thr Asn Ser Gly Asn Arg Phe His Tyr Phe Ser Tyr Gly Val
        1145   1150   1155

Ala Cys Ser Glu Val Glu Ile Asp Cys Leu Thr Gly Asp His Lys
        1160   1165   1170

1409

```
Asn Leu  Arg Thr Asp Ile Val  Met Asp Val Gly Ser  Ser Leu Asn
    1175             1180             1185


Pro Ala  Ile Asp Ile Gly Gln  Val Glu Gly Ala Phe  Val Gln Gly
    1190             1195             1200


Leu Gly  Leu Phe Thr Leu Glu  Glu Leu His Tyr Ser  Pro Glu Gly
    1205             1210             1215


Ser Leu  His Thr Arg Gly Pro  Ser Thr Tyr Lys Ile  Pro Ala Phe
    1220             1225             1230


Gly Ser  Ile Pro Ile Glu Phe  Arg Val Ser Leu Leu  Arg Asp Cys
    1235             1240             1245


Pro Asn  Lys Lys Ala Ile Tyr  Ala Ser Lys Ala Val  Gly Glu Pro
    1250             1255             1260


Pro Leu  Phe Leu Ala Ala Ser  Ile Phe Phe Ala Ile  Lys Asp Ala
    1265             1270             1275


Ile Arg  Ala Ala Arg Ala Gln  His Thr Gly Asn Asn  Val Lys Glu
    1280             1285             1290


Leu Phe  Arg Leu Asp Ser Pro  Ala Thr Pro Glu Lys  Ile Arg Asn
    1295             1300             1305


Ala Cys  Val Asp Lys Phe Thr  Thr Leu Cys Val Thr  Gly Val Pro
    1310             1315             1320


Glu Asn  Cys Lys Pro Trp Ser  Val Arg Val
    1325             1330
```

```
<210>  2993
<211>  415
<212>  PRT
<213>  Homo sapiens

<400>  2993

Met Glu Gly Lys Ala Ile Ala Thr Ser Leu Gly Gly Asp Arg Val Leu
1                 5                 10                15


Ile Phe Pro Cys Ser Pro Arg Ser Ser Phe Val Phe Thr Ser Arg Leu
            20                25                30


Ser Ser Leu Pro Leu Lys Arg Ala Ser Ile Gly Gly Ala Val Ser Cys
```

Ser Gly Val Asn Gly Leu Thr Arg Trp Asn Ser Ile Val Ser Thr Arg
    50   55   60

Arg Leu Val Pro Val Arg Ser Ile Asn Ser Glu Ser Asp Ser Asp Ser
65   70   75   80

Asp Phe Pro His Glu Asn Gln Gln Gly Asn Pro Gly Leu Gly Lys Phe
                85   90   95

Lys Glu Tyr Gln Glu Trp Asp Ser Trp Thr Ala Lys Phe Ser Gly Gly
            100   105   110

Ala Asn Ile Pro Phe Leu Met Leu Gln Leu Pro Gln Ile Ile Leu Asn
        115   120   125

Thr Gln Asn Leu Leu Ala Gly Asn Asn Thr Ala Leu Ser Ala Val Pro
    130   135   140

Trp Leu Gly Met Leu Thr Gly Leu Leu Gly Asn Leu Ser Leu Leu Ser
145   150   155   160

Tyr Phe Ala Lys Lys Arg Glu Lys Glu Ala Ala Val Val Gln Thr Leu
            165   170   175

Gly Val Val Ser Thr His Ile Val Leu Ala Gln Leu Thr Met Ala Glu
            180   185   190

Ala Met Pro Ile Gln Tyr Phe Val Ala Thr Ser Ala Val Val Thr Ile
        195   200   205

Gly Leu Ile Val Asn Cys Leu Tyr Tyr Phe Gly Lys Leu Ser Lys Thr
    210   215   220

Val Trp Gln Leu Trp Glu Asp Val Ile Thr Ile Gly Gly Leu Ser Val
225   230   235   240

Leu Pro Gln Ile Met Trp Ser Thr Phe Val Pro Leu Val Pro Asn Ser
            245   250   255

Ile Leu Pro Gly Thr Thr Ala Phe Gly Ile Ala Val Ala Ala Ile Ile
            260   265   270

Met Ala Arg Thr Gly Lys Leu Ser Glu Lys Gly Val Arg Phe Val Gly
    275   280   285

Ser Leu Ser Gly Trp Thr Ala Thr Leu Met Phe Met Trp Met Pro Val
    290   295   300

Ser Gln Met Trp Thr Asn Phe Leu Asn Pro Asp Asn Ile Lys Gly Leu
305   310   315   320

Ser Ser Ile Thr Met Leu Leu Ser Met Met Gly Asn Gly Leu Met Ile
                325   330   335

Pro Arg Ala Leu Phe Ile Arg Asp Leu Met Trp Leu Thr Gly Ser Leu
            340   345   350

Trp Ala Thr Leu Phe Tyr Gly Tyr Gly Asn Ile Leu Cys Leu Tyr Leu
            355   360   365

Val Asn Cys Thr Ser Gln Ser Phe Phe Val Ala Ala Thr Ile Gly Leu
    370   375   380

Ile Ser Trp Ile Gly Leu Ala Leu Trp Arg Asp Ala Val Ala Tyr Gly
385   390   395   400

His Asn Ser Pro Phe Arg Ser Leu Lys Glu Leu Val Phe Gly Pro
            405   410   415

<210>   2994
<211>   363
<212>   PRT
<213>   Homo sapiens

<400>   2994

Met Ala Gln Thr Pro Ala Phe Asp Lys Pro Lys Val Glu Leu His Val
1   5   10   15

His Leu Asp Gly Ser Ile Lys Pro Glu Thr Ile Leu Tyr Tyr Gly Arg
            20   25   30

Arg Arg Gly Ile Ala Leu Pro Ala Asn Thr Ala Glu Gly Leu Leu Asn
        35   40   45

Val Ile Gly Met Asp Lys Pro Leu Thr Leu Pro Asp Phe Leu Ala Lys
    50   55   60

Phe Asp Tyr Tyr Met Pro Ala Ile Ala Gly Cys Arg Glu Ala Ile Lys
65   70   75   80

```
Arg Ile Ala Tyr Glu Phe Val Glu Met Lys Ala Lys Glu Gly Val Val
              85              90                  95

Tyr Val Glu Val Arg Tyr Ser Pro His Leu Leu Ala Asn Ser Lys Val
             100             105             110

Glu Pro Ile Pro Trp Asn Gln Ala Glu Gly Asp Leu Thr Pro Asp Glu
         115             120             125

Val Val Ala Leu Val Gly Gln Gly Leu Gln Glu Gly Glu Arg Asp Phe
     130             135             140

Gly Val Lys Ala Arg Ser Ile Leu Cys Cys Met Arg His Gln Pro Asn
 145             150             155             160

Trp Ser Pro Lys Val Val Glu Leu Cys Lys Asn Tyr Gln Gln Gln Thr
             165             170             175

Val Val Ala Ile Asp Leu Ala Gly Asp Glu Thr Ile Pro Gly Ser Ser
             180             185             190

Leu Leu Pro Gly His Val Gln Ala Tyr Gln Glu Ala Val Lys Ser Gly
         195             200             205

Ile His Arg Thr Val His Ala Gly Glu Val Gly Ser Ala Glu Val Val
     210             215             220

Lys Glu Ala Val Asp Ile Leu Lys Thr Glu Arg Leu Gly His Gly Tyr
 225             230             235             240

His Thr Leu Glu Asp Gln Ala Leu Tyr Asn Arg Leu Arg Gln Glu Asn
             245             250             255

Met His Phe Glu Ile Cys Pro Trp Ser Ser Tyr Leu Thr Gly Ala Trp
         260             265             270

Lys Pro Asp Thr Glu His Ala Val Ile Arg Leu Lys Asn Asp Gln Ala
         275             280             285

Asn Tyr Ser Leu Asn Thr Asp Asp Pro Leu Ile Phe Lys Ser Thr Leu
 290             295             300

Asp Thr Asp Tyr Gln Met Thr Lys Arg Asp Met Gly Phe Thr Glu Glu
 305             310             315             320

Glu Phe Lys Arg Leu Asn Ile Asn Ala Ala Lys Ser Ser Phe Leu Pro
```

                    325   330   335

Glu Asp Glu Lys Arg Glu Leu Leu Asp Leu Leu Tyr Lys Ala Tyr Gly
            340   345   350

Met Pro Pro Ser Ala Ser Ala Gly Gln Asn Leu
        355   360

<210>   2995
<211>   691
<212>   PRT
<213>   Homo sapiens

<400>   2995

Met Met Arg Asn His Arg Ile Ala Ser Ser Leu Cys Gly Asp Gln Val
1   5   10   15

Phe Ser Lys Lys Lys Lys Lys Lys Lys Asn Asn Met Ala Ala Lys
            20   25   30

Glu Lys Leu Glu Ala Val Leu Asn Val Ala Leu Arg Val Pro Ser Ile
        35   40   45

Met Leu Leu Asp Val Leu Tyr Arg Trp Asp Val Ser Ser Phe Phe Gln
    50   55   60

Gln Ile Gln Arg Ser Ser Leu Ser Asn Asn Pro Leu Phe Gln Tyr Lys
65   70   75   80

Tyr Leu Ala Leu Asn Met His Tyr Val Gly Tyr Ile Leu Ser Val Val
                85   90   95

Leu Leu Thr Leu Pro Arg Gln His Leu Val Gln Leu Tyr Leu Tyr Phe
            100   105   110

Leu Thr Ala Leu Leu Leu Tyr Ala Gly His Gln Ile Ser Arg Asp Tyr
        115   120   125

Val Arg Ser Glu Leu Glu Phe Ala Tyr Glu Gly Pro Met Tyr Leu Glu
    130   135   140

Pro Leu Ser Met Asn Arg Phe Thr Thr Ala Leu Ile Gly Gln Leu Val
145   150   155   160

Val Cys Thr Leu Cys Ser Cys Val Met Lys Thr Lys Gln Ile Trp Leu
            165   170   175

                                    1414

Phe Ser Ala His Met Leu Pro Leu Leu Ala Arg Leu Cys Leu Val Pro
              180   185   190

Leu Glu Thr Ile Val Ile Ile Asn Lys Phe Ala Met Ile Phe Thr Gly
          195   200   205

Leu Glu Val Leu Tyr Phe Leu Gly Ser Asn Leu Leu Val Pro Tyr Asn
      210   215   220

Leu Ala Lys Ser Ala Tyr Arg Glu Leu Val Gln Val Val Glu Val Tyr
225   230   235   240

Gly Leu Leu Ala Leu Gly Met Ser Leu Trp Asn Gln Leu Val Val Pro
              245   250   255

Val Leu Phe Met Val Phe Trp Leu Val Leu Phe Ala Leu Gln Ile Tyr
              260   265   270

Ser Tyr Phe Ser Thr Arg Asp Gln Pro Ala Ser Arg Glu Arg Leu Leu
      275   280   285

Phe Leu Phe Leu Thr Ser Ile Ala Glu Cys Cys Ser Thr Pro Tyr Ser
      290   295   300

Leu Leu Gly Leu Val Phe Thr Val Ser Phe Val Ala Leu Gly Val Leu
305   310   315   320

Thr Leu Cys Lys Phe Tyr Leu Gln Gly Tyr Arg Ala Phe Met Asn Asp
              325   330   335

Pro Ala Met Asn Arg Gly Met Thr Glu Gly Val Thr Leu Leu Ile Leu
              340   345   350

Ala Val Gln Thr Gly Leu Ile Glu Leu Gln Val Val His Arg Ala Phe
      355   360   365

Leu Leu Ser Ile Ile Leu Phe Ile Val Val Ala Ser Ile Leu Gln Ser
      370   375   380

Met Leu Glu Ile Ala Asp Pro Ile Val Leu Ala Leu Gly Ala Ser Arg
385   390   395   400

Asp Lys Ser Leu Trp Lys His Phe Arg Ala Val Ser Leu Cys Leu Phe
              405   410   415

1415

Leu Leu Val Phe Pro Ala Tyr Met Ala Tyr Met Ile Cys Gln Phe Phe
            420   425   430

His Met Asp Phe Trp Leu Leu Ile Ile Ile Ser Ser Ser Ile Leu Thr
        435   440   445

Ser Leu Gln Val Leu Gly Thr Leu Phe Ile Tyr Val Leu Phe Met Val
    450   455   460

Glu Glu Phe Arg Lys Glu Pro Val Glu Asn Met Asp Asp Val Ile Tyr
465   470   475   480

Tyr Val Asn Gly Thr Tyr Arg Leu Leu Glu Phe Leu Val Ala Leu Cys
                485   490   495

Val Val Ala Tyr Gly Val Ser Glu Thr Ile Phe Gly Glu Trp Thr Val
            500   505   510

Met Gly Ser Met Ile Ile Phe Ile His Ser Tyr Tyr Asn Val Trp Leu
        515   520   525

Arg Ala Gln Leu Gly Trp Lys Ser Phe Leu Leu Arg Arg Asp Ala Val
    530   535   540

Asn Lys Ile Lys Ser Leu Pro Ile Ala Thr Lys Glu Gln Leu Glu Lys
545   550   555   560

His Asn Asp Ile Cys Ala Ile Cys Tyr Gln Asp Met Lys Ser Ala Val
            565   570   575

Ile Thr Pro Cys Ser His Phe Phe His Ala Gly Cys Leu Lys Lys Trp
            580   585   590

Leu Tyr Val Gln Glu Thr Cys Pro Leu Cys His Cys His Leu Lys Asn
        595   600   605

Ser Ser Gln Leu Pro Gly Leu Gly Thr Glu Pro Val Leu Gln Pro His
    610   615   620

Ala Gly Ala Glu Gln Asn Val Met Phe Gln Glu Gly Thr Glu Pro Pro
625   630   635   640

Gly Gln Glu His Thr Pro Gly Thr Arg Ile Gln Glu Gly Ser Arg Asp
                645   650   655

Asn Asn Glu Tyr Ile Ala Arg Arg Pro Asp Asn Gln Glu Gly Ala Phe

1416

                    660   665   670

        Asp Pro Lys Glu Tyr Pro His Ser Ala Lys Asp Glu Ala His Pro Val
                675   680   685

        Glu Ser Ala
            690

        <210> 2996
        <211> 390
        <212> PRT
        <213> Homo sapiens

        <400> 2996

        Met Ala Ser Pro Ala Ile Gly Gln Arg Pro Tyr Pro Leu Leu Leu Asp
        1   5   10   15

        Pro Glu Pro Pro Arg Tyr Leu Gln Ser Leu Ser Gly Pro Glu Leu Pro
                    20   25   30

        Pro Pro Pro Pro Asp Arg Ser Ser Arg Leu Cys Val Pro Ala Pro Leu
                35   40   45

        Ser Thr Ala Pro Gly Ala Arg Glu Gly Arg Ser Ala Arg Arg Ala Ala
            50   55   60

        Arg Gly Asn Leu Glu Pro Pro Pro Arg Ala Ser Arg Pro Ala Arg Pro
        65   70   75   80

        Leu Arg Pro Gly Leu Gln Gln Arg Leu Arg Arg Arg Pro Gly Ala Pro
                        85   90   95

        Arg Pro Arg Asp Val Arg Ser Ile Phe Glu Gln Pro Gln Asp Pro Arg
                    100   105   110

        Val Pro Ala Glu Arg Gly Glu Gly His Cys Phe Ala Glu Leu Val Leu
                115   120   125

        Pro Gly Gly Pro Gly Trp Cys Asp Leu Cys Gly Arg Glu Val Leu Arg
            130   135   140

        Gln Ala Leu Arg Cys Thr Asn Cys Lys Phe Thr Cys His Pro Glu Cys
        145   150   155   160

        Arg Ser Leu Ile Gln Leu Asp Cys Ser Gln Gln Glu Gly Leu Ser Arg
                        165   170   175

                                    1417

Asp Arg Pro Ser Pro Glu Ser Thr Leu Thr Val Thr Phe Ser Gln Asn
        180   185   190

Val Cys Lys Pro Val Glu Glu Thr Gln Arg Pro Pro Thr Leu Gln Glu
        195   200   205

Ile Lys Gln Lys Ile Asp Ser Tyr Asn Thr Arg Glu Lys Asn Cys Leu
        210   215   220

Gly Met Lys Leu Ser Glu Asp Gly Thr Tyr Thr Gly Phe Ile Lys Val
225   230   235   240

His Leu Lys Leu Arg Arg Pro Val Thr Val Pro Ala Gly Ile Arg Pro
                245   250   255

Gln Ser Ile Tyr Asp Ala Ile Lys Glu Val Asn Leu Ala Ala Thr Thr
                260   265   270

Asp Lys Arg Thr Ser Phe Tyr Leu Pro Leu Asp Ala Ile Lys Gln Leu
        275   280   285

His Ile Ser Ser Thr Thr Thr Val Ser Glu Val Ile Gln Gly Leu Leu
        290   295   300

Lys Lys Phe Met Val Val Asp Asn Pro Gln Lys Phe Ala Leu Phe Lys
305   310   315   320

Arg Ile His Lys Asp Gly Gln Val Leu Phe Gln Lys Leu Ser Ile Ala
                325   330   335

Asp Arg Pro Leu Tyr Leu Arg Leu Leu Ala Gly Pro Asp Thr Glu Val
                340   345   350

Leu Ser Phe Val Leu Lys Glu Asn Glu Thr Gly Glu Val Glu Trp Asp
        355   360   365

Ala Phe Ser Ile Pro Glu Leu Gln Asn Phe Leu Ser Ser Trp Cys Ile
        370   375   380

Gln Ile Tyr Leu Tyr Tyr
385   390

<210>   2997
<211>   297
<212>   PRT
<213>   Homo sapiens

<400> 2997

Met Thr Thr Pro Arg Asn Ser Val Asn Gly Thr Phe Pro Ala Glu Pro
1   5   10   15

Met Lys Gly Pro Ile Ala Met Gln Ser Gly Pro Lys Pro Leu Phe Arg
            20   25   30

Arg Met Ser Ser Leu Val Gly Pro Thr Gln Ser Phe Phe Met Arg Glu
        35   40   45

Ser Lys Thr Leu Gly Ala Val Gln Ile Met Asn Gly Leu Phe His Ile
    50   55   60

Ala Leu Gly Gly Leu Leu Met Ile Pro Ala Gly Ile Tyr Ala Pro Ile
65   70   75   80

Cys Val Thr Val Trp Tyr Pro Leu Trp Gly Gly Ile Met Tyr Ile Ile
                85   90   95

Ser Gly Ser Leu Leu Ala Ala Thr Glu Lys Asn Ser Arg Lys Cys Leu
            100   105   110

Val Lys Gly Lys Met Ile Met Asn Ser Leu Ser Leu Phe Ala Ala Ile
        115   120   125

Ser Gly Met Ile Leu Ser Ile Met Asp Ile Leu Asn Ile Lys Ile Ser
    130   135   140

His Phe Leu Lys Met Glu Ser Leu Asn Phe Ile Arg Ala His Thr Pro
145   150   155   160

Tyr Ile Asn Ile Tyr Asn Cys Glu Pro Ala Asn Pro Ser Glu Lys Asn
                165   170   175

Ser Pro Ser Thr Gln Tyr Cys Tyr Ser Ile Gln Ser Leu Phe Leu Gly
            180   185   190

Ile Leu Ser Val Met Leu Ile Phe Ala Phe Phe Gln Glu Leu Val Ile
        195   200   205

Ala Gly Ile Val Glu Asn Glu Trp Lys Arg Thr Cys Ser Arg Pro Lys
    210   215   220

Ser Asn Ile Val Leu Leu Ser Ala Glu Glu Lys Lys Glu Gln Thr Ile
225   230   235   240

```
Glu Ile Lys Glu Glu Val Val Gly Leu Thr Glu Thr Ser Ser Gln Pro
            245                     250                 255


Lys Asn Glu Glu Asp Ile Glu Ile Ile Pro Ile Gln Glu Glu Glu Glu
            260                     265                 270


Glu Glu Thr Glu Thr Asn Phe Pro Glu Pro Pro Gln Asp Gln Glu Ser
            275                     280                 285


Ser Pro Ile Glu Asn Asp Ser Ser Pro
        290                     295
```

<210> 2998
<211> 261
<212> PRT
<213> Homo sapiens

<400> 2998

```
Met Ser Trp Lys Lys Ala Leu Arg Ile Pro Gly Gly Leu Arg Ala Ala
1               5                   10                  15


Thr Val Thr Leu Met Leu Ser Met Leu Ser Thr Pro Val Ala Glu Gly
            20                      25                  30


Arg Asp Ser Pro Glu Asp Phe Val Tyr Gln Phe Lys Gly Met Cys Tyr
            35                      40                  45


Phe Thr Asn Gly Thr Glu Arg Val Arg Leu Val Ser Arg Ser Ile Tyr
    50                      55                  60


Asn Arg Glu Glu Ile Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg
65                      70                  75                  80


Ala Val Thr Leu Leu Gly Leu Pro Ala Ala Glu Tyr Trp Asn Ser Gln
                85                      90                  95


Lys Asp Ile Leu Glu Arg Lys Arg Ala Ala Val Asp Arg Val Cys Arg
            100                     105                 110


His Asn Tyr Gln Leu Glu Leu Arg Thr Thr Leu Gln Arg Arg Val Glu
            115                     120                 125


Pro Thr Val Thr Ile Ser Pro Ser Arg Thr Glu Ala Leu Asn His His
            130                     135                 140
```

Asn Leu Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys
145   150   155   160

Val Arg Trp Phe Arg Asn Asp Gln Glu Glu Thr Ala Gly Val Val Ser
                165   170   175

Thr Pro Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met
                180   185   190

Leu Glu Met Thr Pro Gln Arg Gly Asp Val Tyr Thr Cys His Val Glu
            195   200   205

His Pro Ser Leu Gln Ser Pro Ile Thr Val Glu Trp Arg Ala Gln Ser
        210   215   220

Glu Ser Ala Gln Ser Lys Met Leu Ser Gly Ile Gly Gly Phe Val Leu
225   230   235   240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile His His Arg Ser Gln
                245   250   255

Lys Gly Leu Leu His
            260

<210> 2999
<211> 258
<212> PRT
<213> Homo sapiens

<400> 2999

Met Met Val Leu Gln Val Ser Ala Ala Pro Arg Thr Val Ala Leu Thr
1   5   10   15

Ala Leu Leu Met Val Leu Leu Thr Ser Val Val Gln Gly Arg Ala Thr
                20   25   30

Pro Glu Asn Tyr Leu Phe Gln Gly Arg Gln Glu Cys Tyr Ala Phe Asn
            35   40   45

Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg Glu Glu Phe
        50   55   60

Ala Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr Glu Leu
65   70   75   80

Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
                85   90   95

1421

```
     Glu Lys Arg Ala Val Pro Asp Arg Met Cys Arg His Asn Tyr Glu Leu
                 100                 105                 110

     Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg Val Asn Val
                 115                 120                 125

     Ser Pro Ser Lys Lys Gly Pro Leu Gln His His Asn Leu Leu Val Cys
                 130                 135                 140

     His Val Thr Asp Phe Tyr Pro Gly Ser Ile Gln Val Arg Trp Phe Leu
     145                 150                 155                 160

     Asn Gly Gln Glu Glu Thr Ala Gly Val Val Ser Thr Asn Leu Ile Arg
                     165                 170                 175

     Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met Leu Glu Met Thr Pro
                 180                 185                 190

     Gln Gln Gly Asp Val Tyr Thr Cys Gln Val Glu His Thr Ser Leu Asp
                 195                 200                 205

     Ser Pro Val Thr Val Glu Trp Lys Ala Gln Ser Asp Ser Ala Arg Ser
                 210                 215                 220

     Lys Thr Leu Thr Gly Ala Gly Gly Phe Val Leu Gly Leu Ile Ile Cys
     225                 230                 235                 240

     Gly Val Gly Ile Phe Met His Arg Arg Ser Lys Lys Val Gln Arg Gly
                     245                 250                 255

     Ser Ala
```

```
<210> 3000
<211> 175
<212> PRT
<213> Homo sapiens

<400> 3000
```

```
     Met Thr Asp Cys Glu Phe Gly Tyr Ile Tyr Arg Leu Ala Gln Asp Tyr
     1               5                   10                  15

     Leu Gln Cys Val Leu Gln Ile Pro Gln Pro Gly Ser Gly Pro Ser Lys
                 20                  25                  30
```

```
Thr Ser Arg Val Leu Gln Asn Val Ala Phe Ser Val Gln Lys Glu Val
        35                  40                  45

Glu Lys Asn Leu Lys Ser Cys Leu Asp Asn Val Asn Val Val Ser Val
    50                  55                  60

Asp Thr Ala Arg Thr Leu Phe Asn Gln Val Met Glu Lys Glu Phe Glu
65                  70                  75                  80

Asp Gly Ile Ile Asn Trp Gly Arg Ile Val Thr Ile Phe Ala Phe Glu
                85                  90                  95

Gly Ile Leu Ile Lys Lys Leu Leu Arg Gln Gln Ile Ala Pro Asp Val
                100                 105                 110

Asp Thr Tyr Lys Glu Ile Ser Tyr Phe Val Ala Glu Phe Ile Met Asn
        115                 120                 125

Asn Thr Gly Glu Trp Ile Arg Gln Asn Gly Gly Trp Glu Asn Gly Phe
    130                 135                 140

Val Lys Lys Phe Glu Pro Lys Ser Gly Trp Met Thr Phe Leu Glu Val
145                 150                 155                 160

Thr Gly Lys Ile Cys Glu Met Leu Ser Leu Leu Lys Gln Tyr Cys
                165                 170                 175
```

```
<210>  3001
<211>  825
<212>  PRT
<213>  Homo sapiens

<400>  3001
```

```
Met Gly Trp Leu Cys Ser Gly Leu Leu Phe Pro Val Ser Cys Leu Val
1               5                   10                  15

Leu Leu Gln Val Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro
                20                  25                  30

Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met
        35                  40                  45

Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu
    50                  55                  60

Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly
65                  70                  75                  80
```

```
Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala
            85              90              95


Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys
            100             105             110


Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn
            115             120             125


Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Leu Thr Trp Ser
    130             135             140


Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala
145             150             155             160


Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn
            165             170             175


Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys
            180             185             190


Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Cys Tyr
            195             200             205


Asn Thr Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser
    210             215             220


Tyr Arg Glu Pro Phe Glu Gln His Leu Leu Leu Gly Val Ser Val Ser
225             230             235             240


Cys Ile Val Ile Leu Ala Val Cys Leu Leu Cys Tyr Val Ser Ile Thr
            245             250             255


Lys Ile Lys Lys Glu Trp Trp Asp Gln Ile Pro Asn Pro Ala Arg Ser
            260             265             270


Arg Leu Val Ala Ile Ile Ile Gln Asp Ala Gln Gly Ser Gln Trp Glu
            275             280             285


Lys Arg Ser Arg Gly Gln Glu Pro Ala Lys Cys Pro His Trp Lys Asn
    290             295             300


Cys Leu Thr Lys Leu Leu Pro Cys Phe Leu Glu His Asn Met Lys Arg
305             310             315             320
```

```
Asp Glu Asp Pro His Lys Ala Ala Lys Glu Met Pro Phe Gln Gly Ser
            325              330              335

Gly Lys Ser Ala Trp Cys Pro Val Glu Ile Ser Lys Thr Val Leu Trp
            340              345              350

Pro Glu Ser Ile Ser Val Val Arg Cys Val Glu Leu Phe Glu Ala Pro
            355              360              365

Val Glu Cys Glu Glu Glu Glu Glu Val Glu Glu Glu Lys Gly Ser Phe
    370              375              380

Cys Ala Ser Pro Glu Ser Ser Arg Asp Asp Phe Gln Glu Gly Arg Glu
385              390              395              400

Gly Ile Val Ala Arg Leu Thr Glu Ser Leu Phe Leu Asp Leu Leu Gly
            405              410              415

Glu Glu Asn Gly Gly Phe Cys Gln Gln Asp Met Gly Glu Ser Cys Leu
            420              425              430

Leu Pro Pro Ser Gly Ser Thr Ser Ala His Met Pro Trp Asp Glu Phe
            435              440              445

Pro Ser Ala Gly Pro Lys Glu Ala Pro Pro Trp Gly Lys Glu Gln Pro
    450              455              460

Leu His Leu Glu Pro Ser Pro Pro Ala Ser Pro Thr Gln Ser Pro Asp
465              470              475              480

Asn Leu Thr Cys Thr Glu Thr Pro Leu Val Ile Ala Gly Asn Pro Ala
            485              490              495

Tyr Arg Ser Phe Ser Asn Ser Leu Ser Gln Ser Pro Cys Pro Arg Glu
            500              505              510

Leu Gly Pro Asp Pro Leu Leu Ala Arg His Leu Glu Glu Val Glu Pro
            515              520              525

Glu Met Pro Cys Val Pro Gln Leu Ser Glu Pro Thr Thr Val Pro Gln
    530              535              540

Pro Glu Pro Glu Thr Trp Glu Gln Ile Leu Arg Arg Asn Val Leu Gln
545              550              555              560
```

His Gly Ala Ala Ala Ala Pro Val Ser Ala Pro Thr Ser Gly Tyr Gln
              565   570   575

Glu Phe Val His Ala Val Glu Gln Gly Gly Thr Gln Ala Ser Ala Val
              580   585   590

Val Gly Leu Gly Pro Pro Gly Glu Ala Gly Tyr Lys Ala Phe Ser Ser
              595   600   605

Leu Leu Ala Ser Ser Ala Val Ser Pro Glu Lys Cys Gly Phe Gly Ala
              610   615   620

Ser Ser Gly Glu Glu Gly Tyr Lys Pro Phe Gln Asp Leu Ile Pro Gly
625   630   635   640

Cys Pro Gly Asp Pro Ala Pro Val Pro Val Pro Leu Phe Thr Phe Gly
              645   650   655

Leu Asp Arg Glu Pro Pro Arg Ser Pro Gln Ser Ser His Leu Pro Ser
              660   665   670

Ser Ser Pro Glu His Leu Gly Leu Glu Pro Gly Glu Lys Val Glu Asp
              675   680   685

Met Pro Lys Pro Pro Leu Pro Gln Glu Gln Ala Thr Asp Pro Leu Val
              690   695   700

Asp Ser Leu Gly Ser Gly Ile Val Tyr Ser Ala Leu Thr Cys His Leu
705   710   715   720

Cys Gly His Leu Lys Gln Cys His Gly Gln Glu Asp Gly Gly Gln Thr
              725   730   735

Pro Val Met Ala Ser Pro Cys Cys Gly Cys Cys Cys Gly Asp Arg Ser
              740   745   750

Ser Pro Pro Thr Thr Pro Leu Arg Ala Pro Asp Pro Ser Pro Gly Gly
              755   760   765

Val Pro Leu Glu Ala Ser Leu Cys Pro Ala Ser Leu Ala Pro Ser Gly
              770   775   780

Ile Ser Glu Lys Ser Lys Ser Ser Ser Ser Phe His Pro Ala Pro Gly
785   790   795   800

Asn Ala Gln Ser Ser Ser Gln Thr Pro Lys Ile Val Asn Phe Val Ser

                    805   810   815

        Val Gly Pro Thr Tyr Met Arg Val Ser
                    820   825

<210>   3002
<211>   285
<212>   PRT
<213>   Homo sapiens

<400>   3002

Met Asp Asp Ser Thr Glu Arg Glu Gln Ser Arg Leu Thr Ser Cys Leu
1   5   10   15

Lys Lys Arg Glu Glu Met Lys Leu Lys Glu Cys Val Ser Ile Leu Pro
                20   25   30

Arg Lys Glu Ser Pro Ser Val Arg Ser Ser Lys Asp Gly Lys Leu Leu
            35   40   45

Ala Ala Thr Leu Leu Leu Ala Leu Leu Ser Cys Cys Leu Thr Val Val
        50   55   60

Ser Phe Tyr Gln Val Ala Ala Leu Gln Gly Asp Leu Ala Ser Leu Arg
65   70   75   80

Ala Glu Leu Gln Gly His His Ala Glu Lys Leu Pro Ala Gly Ala Gly
                85   90   95

Ala Pro Lys Ala Gly Leu Glu Glu Ala Pro Ala Val Thr Ala Gly Leu
            100   105   110

Lys Ile Phe Glu Pro Pro Ala Pro Gly Glu Gly Asn Ser Ser Gln Asn
        115   120   125

Ser Arg Asn Lys Arg Ala Val Gln Gly Pro Glu Glu Thr Val Thr Gln
    130   135   140

Asp Cys Leu Gln Leu Ile Ala Asp Ser Glu Thr Pro Thr Ile Gln Lys
145   150   155   160

Gly Ser Tyr Thr Phe Val Pro Trp Leu Leu Ser Phe Lys Arg Gly Ser
                165   170   175

Ala Leu Glu Glu Lys Glu Asn Lys Ile Leu Val Lys Glu Thr Gly Tyr
            180   185   190

                            1427

```
Phe Phe Ile Tyr Gly Gln Val Leu Tyr Thr Asp Lys Thr Tyr Ala Met
        195                 200                 205

Gly His Leu Ile Gln Arg Lys Lys Val His Val Phe Gly Asp Glu Leu
        210                 215                 220

Ser Leu Val Thr Leu Phe Arg Cys Ile Gln Asn Met Pro Glu Thr Leu
225                 230                 235                 240

Pro Asn Asn Ser Cys Tyr Ser Ala Gly Ile Ala Lys Leu Glu Glu Gly
                245                 250                 255

Asp Glu Leu Gln Leu Ala Ile Pro Arg Glu Asn Ala Gln Ile Ser Leu
        260                 265                 270

Asp Gly Asp Val Thr Phe Phe Gly Ala Leu Lys Leu Leu
        275                 280                 285
```

```
<210>  3003
<211>  444
<212>  PRT
<213>  Homo sapiens

<400>  3003
```

```
Met Ala Val Thr Thr Arg Leu Thr Arg Leu His Glu Lys Ile Leu Gln
1               5                   10                  15

Asn His Phe Gly Gly Lys Arg Leu Ser Leu Leu Tyr Lys Gly Ser Val
        20                  25                  30

His Gly Phe Arg Asn Gly Val Leu Leu Asp Arg Cys Cys Asn Gln Gly
        35                  40                  45

Pro Thr Leu Thr Val Ile Tyr Ser Glu Asp His Ile Ile Gly Ala Tyr
    50                  55                  60

Ala Glu Glu Ser Tyr Gln Glu Gly Lys Tyr Ala Ser Ile Ile Leu Phe
65                  70                  75                  80

Ala Leu Gln Asp Thr Lys Ile Ser Glu Trp Lys Leu Gly Leu Cys Thr
                85                  90                  95

Pro Glu Thr Leu Phe Cys Cys Asp Val Thr Lys Tyr Asn Ser Pro Thr
        100                 105                 110

Asn Phe Gln Ile Asp Gly Arg Asn Arg Lys Val Ile Met Asp Leu Lys
```

```
                    115                    120                    125
```

```
Thr Met Glu Asn Leu Gly Leu Ala Gln Asn Cys Thr Ile Ser Ile Gln
    130                135                140

Asp Tyr Glu Val Phe Arg Cys Glu Asp Ser Leu Asp Glu Arg Lys Ile
145                150                155                160

Lys Gly Val Ile Glu Leu Arg Lys Ser Leu Leu Ser Ala Leu Arg Thr
                165                170                175

Tyr Glu Pro Tyr Gly Ser Leu Val Gln Gln Ile Arg Ile Leu Leu Leu
            180                185                190

Gly Pro Ile Gly Ala Gly Lys Ser Ser Phe Phe Asn Ser Val Arg Ser
            195                200                205

Val Phe Gln Gly His Val Thr His Gln Ala Leu Val Gly Thr Asn Thr
    210                215                220

Thr Gly Ile Ser Glu Lys Tyr Arg Thr Tyr Ser Ile Arg Asp Gly Lys
225                230                235                240

Asp Gly Lys Tyr Leu Pro Phe Ile Leu Cys Asp Ser Leu Gly Leu Ser
            245                250                255

Glu Lys Glu Gly Gly Leu Cys Arg Asp Asp Ile Phe Tyr Ile Leu Asn
            260                265                270

Gly Asn Ile Arg Asp Arg Tyr Gln Phe Asn Pro Met Glu Ser Ile Lys
            275                280                285

Leu Asn His His Asp Tyr Ile Asp Ser Pro Ser Leu Lys Asp Arg Ile
    290                295                300

His Cys Val Ala Phe Val Phe Asp Ala Ser Ser Ile Gln Tyr Phe Ser
305                310                315                320

Ser Gln Met Ile Val Lys Ile Lys Arg Ile Arg Arg Glu Leu Val Asn
            325                330                335

Ala Gly Val Val His Val Ala Leu Leu Thr His Val Asp Ser Met Asp
            340                345                350

Leu Ile Thr Lys Gly Asp Leu Ile Glu Ile Glu Arg Cys Glu Pro Val
    355                360                365
```

```
Arg Ser Lys Leu Glu Glu Val Gln Arg Lys Leu Gly Phe Ala Leu Ser
    370             375             380

Asp Ile Ser Val Val Ser Asn Tyr Ser Ser Glu Trp Glu Leu Asp Pro
385             390             395             400

Val Lys Asp Val Leu Ile Leu Ser Ala Leu Arg Arg Met Leu Trp Ala
            405             410             415

Ala Asp Asp Phe Leu Glu Asp Leu Pro Phe Glu Gln Ile Gly Asn Leu
            420             425             430

Arg Glu Glu Ile Ile Asn Cys Ala Gln Gly Lys Lys
        435             440
```

```
<210>   3004
<211>   432
<212>   PRT
<213>   Homo sapiens

<400>   3004
```

```
Met Gly Pro Ala Gly Ser Leu Leu Gly Ser Gly Gln Met Gln Ile Thr
1               5               10              15

Leu Trp Gly Ser Leu Ala Ala Val Ala Ile Phe Phe Val Ile Thr Phe
            20              25              30

Leu Ile Phe Pro Cys Ser Ser Cys Asp Arg Glu Lys Lys Pro Arg Gln
        35              40              45

His Ser Gly Asp His Glu Asn Leu Met Asn Val Pro Ser Asp Lys Glu
    50              55              60

Met Phe Ser Arg Ser Val Thr Ser Leu Ala Thr Asp Ala Pro Ala Ser
65              70              75              80

Ser Glu Gln Asn Gly Ala Leu Thr Asn Gly Asp Ile Leu Ser Glu Asp
                85              90              95

Ser Thr Leu Thr Cys Met Gln His Tyr Glu Glu Val Gln Thr Ser Ala
            100             105             110

Ser Asp Leu Leu Asp Ser Gln Asp Ser Thr Gly Lys Pro Lys Cys His
            115             120             125
```

Gln Ser Arg Glu Leu Pro Arg Ile Pro Pro Glu Ser Ala Val Asp Thr
    130   135   140

Met Leu Thr Ala Arg Ser Val Asp Gly Asp Gln Gly Leu Gly Met Glu
145   150   155   160

Gly Pro Tyr Glu Val Leu Lys Asp Ser Ser Ser Gln Glu Asn Met Val
            165   170   175

Glu Asp Cys Leu Tyr Glu Thr Val Lys Glu Ile Lys Glu Val Ala Ala
        180   185   190

Ala Ala His Leu Glu Lys Gly His Ser Gly Lys Ala Lys Ser Thr Ser
        195   200   205

Ala Ser Lys Glu Leu Pro Gly Pro Gln Thr Glu Gly Lys Ala Glu Phe
    210   215   220

Ala Glu Tyr Ala Ser Val Asp Arg Asn Lys Lys Cys Arg Gln Ser Val
225   230   235   240

Asn Val Glu Ser Ile Leu Gly Asn Ser Cys Asp Pro Glu Glu Glu Ala
            245   250   255

Pro Pro Pro Val Pro Val Lys Leu Leu Asp Glu Asn Glu Asn Leu Gln
            260   265   270

Glu Lys Glu Gly Gly Glu Ala Glu Glu Ser Ala Thr Asp Thr Thr Ser
    275   280   285

Glu Thr Asn Lys Arg Phe Ser Ser Leu Ser Tyr Lys Ser Arg Glu Glu
    290   295   300

Asp Pro Thr Leu Thr Glu Glu Ile Ser Ala Met Tyr Ser Ser Val
305   310   315   320

Asn Lys Pro Gly Gln Leu Val Asn Lys Ser Gly Gln Ser Leu Thr Val
            325   330   335

Pro Glu Ser Thr Tyr Thr Ser Ile Gln Gly Asp Pro Gln Arg Ser Pro
            340   345   350

Ser Ser Cys Asn Asp Leu Tyr Ala Thr Val Lys Asp Phe Glu Lys Thr
            355   360   365

Pro Asn Ser Thr Leu Pro Pro Ala Gly Arg Pro Ser Glu Glu Pro Glu

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370   375   380

Pro Asp Tyr Glu Ala Ile Gln Thr Leu Asn Arg Glu Glu Glu Lys Ala
385   390   395   400

Thr Leu Gly Thr Asn Gly His His Gly Leu Val Pro Lys Glu Asn Asp
                405   410   415

Tyr Glu Ser Ile Ser Asp Leu Gln Gln Gly Arg Asp Ile Thr Arg Leu
        420   425   430

<210> 3005
<211> 501
<212> PRT
<213> Homo sapiens

<400> 3005

Met Ile Ile Ser His Phe Pro Lys Cys Val Ala Val Phe Ala Leu Leu
1   5   10   15

Ala Leu Ser Val Gly Ala Leu Asp Thr Phe Ile Ala Ala Val Tyr Glu
            20   25   30

His Ala Val Ile Leu Pro Asn Arg Thr Glu Thr Pro Val Ser Lys Glu
        35   40   45

Glu Ala Leu Leu Leu Met Asn Lys Asn Ile Asp Val Leu Glu Lys Ala
        50   55   60

Val Lys Leu Ala Ala Lys Gln Gly Ala His Ile Ile Val Thr Pro Glu
65   70   75   80

Asp Gly Ile Tyr Gly Trp Ile Phe Thr Arg Glu Ser Ile Tyr Pro Tyr
                85   90   95

Leu Glu Asp Ile Pro Asp Pro Gly Val Asn Trp Ile Pro Cys Arg Asp
                100   105   110

Pro Trp Arg Phe Gly Asn Thr Pro Val Gln Gln Arg Leu Ser Cys Leu
            115   120   125

Ala Lys Asp Asn Ser Ile Tyr Val Val Ala Asn Ile Gly Asp Lys Lys
        130   135   140

Pro Cys Asn Ala Ser Asp Ser Gln Cys Pro Pro Asp Gly Arg Tyr Gln
145   150   155   160

Tyr Asn Thr Asp Val Val Phe Asp Ser Gln Gly Lys Leu Leu Ala Arg
            165   170   175

Tyr His Lys Tyr Asn Leu Phe Ala Pro Glu Ile Gln Phe Asp Phe Pro
            180   185   190

Lys Asp Ser Glu Leu Val Thr Phe Asp Thr Pro Phe Gly Lys Phe Gly
            195   200   205

Ile Phe Thr Cys Phe Asp Ile Phe Ser His Asp Pro Ala Ala Val Val
    210   215   220

Val Asp Glu Val Ser Ile Asp Ser Ile Leu Tyr Pro Thr Ala Trp Tyr
225   230   235   240

Asn Thr Leu Pro Leu Leu Ser Ala Val Pro Phe His Ser Ala Trp Ala
            245   250   255

Lys Ala Met Gly Val Asn Leu Leu Ala Ala Asn Thr His Asn Thr Ser
            260   265   270

Met His Met Thr Gly Ser Gly Ile Tyr Ala Pro Glu Ala Val Lys Val
            275   280   285

Tyr His Tyr Asp Met Glu Thr Glu Ser Gly Gln Leu Leu Leu Ser Glu
    290   295   300

Leu Lys Ser Arg Pro Arg Arg Glu Pro Thr Tyr Pro Ala Ala Val Asp
305   310   315   320

Trp His Ala Tyr Ala Ser Ser Val Lys Pro Phe Ser Ser Glu Gln Ser
            325   330   335

Asp Phe Leu Gly Met Ile Tyr Phe Asp Glu Phe Thr Phe Thr Lys Leu
            340   345   350

Lys Arg Asn Thr Gly Asn Tyr Thr Ala Cys Gln Lys Asp Leu Cys Cys
            355   360   365

His Leu Thr Tyr Lys Met Ser Glu Lys Arg Thr Asp Glu Ile Tyr Ala
    370   375   380

Leu Gly Ala Phe Asp Gly Leu His Thr Val Glu Gly Gln Tyr Tyr Leu
385   390   395   400

Gln Ile Cys Ala Leu Leu Lys Cys Gln Thr Thr Asp Leu Glu Thr Cys
              405   410   415

Gly Glu Pro Val Gly Ser Ala Phe Thr Lys Phe Glu Asp Phe Ser Leu
              420   425   430

Ser Gly Thr Phe Gly Thr Arg Tyr Val Phe Pro Gln Ile Ile Leu Ser
              435   440   445

Gly Ser Gln Leu Ala Pro Glu Arg His Tyr Glu Ile Ser Arg Asp Gly
              450   455   460

Arg Leu Arg Ser Arg Ser Gly Ala Pro Leu Pro Val Leu Val Met Ala
465   470   475   480

Leu Tyr Gly Arg Val Phe Glu Lys Asp Pro Pro Arg Leu Gly Gln Gly
                  485   490   495

Ser Gly Lys Phe Gln
              500

<210>   3006
<211>   329
<212>   PRT
<213>   Homo sapiens

<400>   3006

Met Trp Gly Leu Lys Val Leu Leu Leu Pro Val Val Ser Phe Ala Leu
1   5   10   15

Tyr Pro Glu Glu Ile Leu Asp Thr His Trp Glu Leu Trp Lys Lys Thr
              20   25   30

His Arg Lys Gln Tyr Asn Asn Lys Val Asp Glu Ile Ser Arg Arg Leu
              35   40   45

Ile Trp Glu Lys Asn Leu Lys Tyr Ile Ser Ile His Asn Leu Glu Ala
50   55   60

Ser Leu Gly Val His Thr Tyr Glu Leu Ala Met Asn His Leu Gly Asp
65   70   75   80

Met Thr Ser Glu Glu Val Val Gln Lys Met Thr Gly Leu Lys Val Pro
                  85   90   95

Leu Ser His Ser Arg Ser Asn Asp Thr Leu Tyr Ile Pro Glu Trp Glu
              100   105   110

1434

```
Gly Arg Ala Pro Asp Ser Val Asp Tyr Arg Lys Lys Gly Tyr Val Thr
        115             120             125

Pro Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ser
    130             135             140

Val Gly Ala Leu Glu Gly Gln Leu Lys Lys Lys Thr Gly Lys Leu Leu
145             150             155             160

Asn Leu Ser Pro Gln Asn Leu Val Asp Cys Val Ser Glu Asn Asp Gly
            165             170             175

Cys Gly Gly Gly Tyr Met Thr Asn Ala Phe Gln Tyr Val Gln Lys Asn
            180             185             190

Arg Gly Ile Asp Ser Glu Asp Ala Tyr Pro Tyr Val Gly Gln Glu Glu
        195             200             205

Ser Cys Met Tyr Asn Pro Thr Gly Lys Ala Ala Lys Cys Arg Gly Tyr
    210             215             220

Arg Glu Ile Pro Glu Gly Asn Glu Lys Ala Leu Lys Arg Ala Val Ala
225             230             235             240

Arg Val Gly Pro Val Ser Val Ala Ile Asp Ala Ser Leu Thr Ser Phe
            245             250             255

Gln Phe Tyr Ser Lys Gly Val Tyr Tyr Asp Glu Ser Cys Asn Ser Asp
            260             265             270

Asn Leu Asn His Ala Val Leu Ala Val Gly Tyr Gly Ile Gln Lys Gly
            275             280             285

Asn Lys His Trp Ile Ile Lys Asn Ser Trp Gly Glu Asn Trp Gly Asn
    290             295             300

Lys Gly Tyr Ile Leu Met Ala Arg Asn Lys Asn Asn Ala Cys Gly Ile
305             310             315             320

Ala Asn Leu Ala Ser Phe Pro Lys Met
            325
```

```
<210>  3007
<211>  1170
<212>  PRT
```

<213> Homo sapiens

<400> 3007

```
Met Lys Asp Ser Cys Ile Thr Val Met Ala Met Ala Leu Leu Ser Gly
1               5                   10                  15

Phe Phe Phe Phe Ala Pro Ala Ser Ser Tyr Asn Leu Asp Val Arg Gly
            20                  25                  30

Ala Arg Ser Phe Ser Pro Pro Arg Ala Gly Arg His Phe Gly Tyr Arg
        35                  40                  45

Val Leu Gln Val Gly Asn Gly Val Ile Val Gly Ala Pro Gly Glu Gly
    50                  55                  60

Asn Ser Thr Gly Ser Leu Tyr Gln Cys Gln Ser Gly Thr Gly His Cys
65                  70                  75                  80

Leu Pro Val Thr Leu Arg Gly Ser Asn Tyr Thr Ser Lys Tyr Leu Gly
            85                  90                  95

Met Thr Leu Ala Thr Asp Pro Thr Asp Gly Ser Ile Leu Ala Cys Asp
            100                 105                 110

Pro Gly Leu Ser Arg Thr Cys Asp Gln Asn Thr Tyr Leu Ser Gly Leu
        115                 120                 125

Cys Tyr Leu Phe Arg Gln Asn Leu Gln Gly Pro Met Leu Gln Gly Arg
    130                 135                 140

Pro Gly Phe Gln Glu Cys Ile Lys Gly Asn Val Asp Leu Val Phe Leu
145                 150                 155                 160

Phe Asp Gly Ser Met Ser Leu Gln Pro Asp Glu Phe Gln Lys Ile Leu
            165                 170                 175

Asp Phe Met Lys Asp Val Met Lys Lys Leu Ser Asn Thr Ser Tyr Gln
        180                 185                 190

Phe Ala Ala Val Gln Phe Ser Thr Ser Tyr Lys Thr Glu Phe Asp Phe
    195                 200                 205

Ser Asp Tyr Val Lys Trp Lys Asp Pro Asp Ala Leu Leu Lys His Val
210                 215                 220

Lys His Met Leu Leu Leu Thr Asn Thr Phe Gly Ala Ile Asn Tyr Val
```

225   230   235   240

Ala Thr Glu Val Phe Arg Glu Glu Leu Gly Ala Arg Pro Asp Ala Thr
                    245   250   255

Lys Val Leu Ile Ile Ile Thr Asp Gly Glu Ala Thr Asp Ser Gly Asn
                260   265   270

Ile Asp Ala Ala Lys Asp Ile Ile Arg Tyr Ile Ile Gly Ile Gly Lys
            275   280   285

His Phe Gln Thr Lys Glu Ser Gln Glu Thr Leu His Lys Phe Ala Ser
    290   295   300

Lys Pro Ala Ser Glu Phe Val Lys Ile Leu Asp Thr Phe Glu Lys Leu
305   310   315   320

Lys Asp Leu Phe Thr Glu Leu Gln Lys Lys Ile Tyr Val Ile Glu Gly
                325   330   335

Thr Ser Lys Gln Asp Leu Thr Ser Phe Asn Met Glu Leu Ser Ser Ser
            340   345   350

Gly Ile Ser Ala Asp Leu Ser Arg Gly His Ala Val Val Gly Ala Val
        355   360   365

Gly Ala Lys Asp Trp Ala Gly Gly Phe Leu Asp Leu Lys Ala Asp Leu
    370   375   380

Gln Asp Asp Thr Phe Ile Gly Asn Glu Pro Leu Thr Pro Glu Val Arg
385   390   395   400

Ala Gly Tyr Leu Gly Tyr Thr Val Thr Trp Leu Pro Ser Arg Gln Lys
                405   410   415

Thr Ser Leu Leu Ala Ser Gly Ala Pro Arg Tyr Gln His Met Gly Arg
            420   425   430

Val Leu Leu Phe Gln Glu Pro Gln Gly Gly Gly His Trp Ser Gln Val
    ·   435   440   445

Gln Thr Ile His Gly Thr Gln Ile Gly Ser Tyr Phe Gly Gly Glu Leu
    450   455   460

Cys Gly Val Asp Val Asp Gln Asp Gly Glu Thr Glu Leu Leu Leu Ile
465   470   475   480

```
Gly Ala Pro Leu Phe Tyr Gly Glu Gln Arg Gly Gly Arg Val Phe Ile
             485                 490                 495

Tyr Gln Arg Arg Gln Leu Gly Phe Glu Glu Val Ser Glu Leu Gln Gly
         500                 505                 510

Asp Pro Gly Tyr Pro Leu Gly Arg Phe Gly Glu Ala Ile Thr Ala Leu
         515                 520                 525

Thr Asp Ile Asn Gly Asp Gly Leu Val Asp Val Ala Val Gly Ala Pro
         530                 535                 540

Leu Glu Glu Gln Gly Ala Val Tyr Ile Phe Asn Gly Arg His Gly Gly
545                 550                 555                 560

Leu Ser Pro Gln Pro Ser Gln Arg Ile Glu Gly Thr Gln Val Leu Ser
             565                 570                 575

Gly Ile Gln Trp Phe Gly Arg Ser Ile His Gly Val Lys Asp Leu Glu
             580                 585                 590

Gly Asp Gly Leu Ala Asp Val Ala Val Gly Ala Glu Ser Gln Met Ile
         595                 600                 605

Val Leu Ser Ser Arg Pro Val Val Asp Met Val Thr Leu Met Ser Phe
    610                 615                 620

Ser Pro Ala Glu Ile Pro Val His Glu Val Glu Cys Ser Tyr Ser Thr
625                 630                 635                 640

Ser Asn Lys Met Lys Glu Gly Val Asn Ile Thr Ile Cys Phe Gln Ile
             645                 650                 655

Lys Ser Leu Tyr Pro Gln Phe Gln Gly Arg Leu Val Ala Asn Leu Thr
             660                 665                 670

Tyr Thr Leu Gln Leu Asp Gly His Arg Thr Arg Arg Arg Gly Leu Phe
         675                 680                 685

Pro Gly Gly Arg His Glu Leu Arg Arg Asn Ile Ala Val Thr Thr Ser
690                 695                 700

Met Ser Cys Thr Asp Phe Ser Phe His Phe Pro Val Cys Val Gln Asp
705                 710                 715                 720
```

                                    1438

Leu Ile Ser Pro Ile Asn Val Ser Leu Asn Phe Ser Leu Trp Glu Glu
            725   730   735

Glu Gly Thr Pro Arg Asp Gln Arg Ala Gln Gly Lys Asp Ile Pro Pro
            740   745   750

Ile Leu Arg Pro Ser Leu His Ser Glu Thr Trp Glu Ile Pro Phe Glu
            755   760   765

Lys Asn Cys Gly Glu Asp Lys Lys Cys Glu Ala Asn Leu Arg Val Ser
    770   775   780

Phe Ser Pro Ala Arg Ser Arg Ala Leu Arg Leu Thr Ala Phe Ala Ser
785   790   795   800

Leu Ser Val Glu Leu Ser Leu Ser Asn Leu Glu Glu Asp Ala Tyr Trp
            805   810   815

Val Gln Leu Asp Leu His Phe Pro Pro Gly Leu Ser Phe Arg Lys Val
            820   825   830

Glu Met Leu Lys Pro His Ser Gln Ile Pro Val Ser Cys Glu Glu Leu
            835   840   845

Pro Glu Glu Ser Arg Leu Leu Ser Arg Ala Leu Ser Cys Asn Val Ser
    850   855   860

Ser Pro Ile Phe Lys Ala Gly His Ser Val Ala Leu Gln Met Met Phe
865. .   870   875   880

Asn Thr Leu Val Asn Ser Ser Trp Gly Asp Ser Val Glu Leu His Ala
            885   890   895

Asn Val Thr Cys Asn Asn Glu Asp Ser Asp Leu Leu Glu Asp Asn Ser
            900   905   910

Ala Thr Thr Ile Ile Pro Ile Leu Tyr Pro Ile Asn Ile Leu Ile Gln
            915   920   925

Asp Gln Glu Asp Ser Thr Leu Tyr Val Ser Phe Thr Pro Lys Gly Pro
    930   935   940

Lys Ile His Gln Val Lys His Met Tyr Gln Val Arg Ile Gln Pro Ser
945   950   955   960

```
Ile His Asp His Asn Ile Pro Thr Leu Glu Ala Val Val Gly Val Pro
            965                 970                 975

Gln Pro Pro Ser Glu Gly Pro Ile Thr His Gln Trp Ser Val Gln Met
            980                 985                 990

Glu Pro Pro Val Pro Cys His Tyr Glu Asp Leu Glu Arg Leu Pro Asp
            995                 1000                1005

Ala Ala Glu Pro Cys Leu Pro Gly Ala Leu Phe Arg Cys Pro Val
        1010                1015                1020

Val Phe Arg Gln Glu Ile Leu Val Gln Val Ile Gly Thr Leu Glu
        1025                1030                1035

Leu Val Gly Glu Ile Glu Ala Ser Ser Met Phe Ser Leu Cys Ser
        1040                1045                1050

Ser Leu Ser Ile Ser Phe Asn Ser Ser Lys His Phe His Leu Tyr
        1055                1060                1065

Gly Ser Asn Ala Ser Leu Ala Gln Val Val Met Lys Val Asp Val
        1070                1075                1080

Val Tyr Glu Lys Gln Met Leu Tyr Leu Tyr Val Leu Ser Gly Ile
        1085                1090                1095

Gly Gly Leu Leu Leu Leu Leu Leu Ile Phe Ile Val Leu Tyr Lys
        1100                1105                1110

Val Gly Phe Phe Lys Arg Asn Leu Lys Glu Lys Met Glu Ala Gly
        1115                1120                1125

Arg Gly Val Pro Asn Gly Ile Pro Ala Glu Asp Ser Glu Gln Leu
        1130                1135                1140

Ala Ser Gly Gln Glu Ala Gly Asp Pro Gly Cys Leu Lys Pro Leu
        1145                1150                1155

His Glu Lys Asp Ser Glu Ser Gly Gly Gly Lys Asp
        1160                1165                1170
```

<400> 3008

Met Ala Thr Asn Pro Gln Pro Gln Pro Pro Pro Pro Ala Pro Pro Pro
1   5   10   15

Pro Pro Pro Gln Pro Gln Pro Gln Pro Pro Pro Pro Pro Gly Pro
            20   25   30

Gly Ala Gly Pro Gly Ala Gly Gly Ala Gly Gly Ala Gly Ala Gly Ala
        35   40   45

Gly Asp Pro Gln Leu Val Ala Met Ile Val Asn His Leu Lys Ser Gln
    50   55   60

Gly Leu Phe Asp Gln Phe Arg Arg Asp Cys Leu Ala Asp Val Asp Thr
65   70   75   80

Lys Pro Ala Tyr Gln Asn Leu Arg Gln Arg Val Asp Asn Phe Val Ala
            85   90   95

Asn His Leu Ala Thr His Thr Trp Ser Pro His Leu Asn Lys Asn Gln
        100   105   110

Leu Arg Asn Asn Ile Arg Gln Gln Val Leu Lys Ser Gly Met Leu Glu
        115   120   125

Ser Gly Ile Asp Arg Ile Ile Ser Gln Val Val Asp Pro Lys Ile Asn
    130   135   140

His Thr Phe Arg Pro Gln Val Glu Lys Ala Val His Glu Phe Leu Ala
145   150   155   160

Thr Leu Asn His Lys Glu Glu Gly Ser Gly Asn Thr Ala Pro Asp Asp
            165   170   175

Glu Lys Pro Asp Thr Ser Leu Ile Thr Gln Gly Val Pro Thr Pro Gly
            180   185   190

Pro Ser Ala Asn Val Ala Asn Asp Ala Met Ser Ile Leu Glu Thr Ile
        195   200   205

Thr Ser Leu Asn Gln Glu Ala Ser Ala Ala Arg Ala Ser Thr Glu Thr
    210   215   220

Ser Asn Ala Lys Thr Ser Glu Arg Ala Ser Lys Lys Leu Pro Ser Gln
225   230   235   240

1441

Pro Thr Thr Asp Thr Ser Thr Asp Lys Glu Arg Thr Ser Glu Asp Met
              245   250   255

Ala Asp Lys Glu Lys Ser Thr Ala Asp Ser Gly Gly Glu Gly Leu Glu
              260   265   270

Thr Ala Pro Lys Ser Glu Glu Phe Ser Asp Leu Pro Cys Pro Val Glu
              275   280   285

Glu Ile Lys Asn Tyr Thr Lys Glu His Asn Asn Leu Ile Leu Leu Asn
       290   295   300

Lys Asp Val Gln Gln Glu Ser Ser Glu Gln Lys Asn Lys Ser Thr Asp
305   310   315   320

Lys Gly Glu Lys Lys Pro Asp Ser Asn Glu Lys Gly Glu Arg Lys Lys
              325   330   335

Glu Lys Lys Glu Lys Thr Glu Lys Lys Phe Asp His Ser Lys Lys Ser
              340   345   350

Glu Asp Thr Gln Lys Val Lys Asp Glu Lys Gln Ala Lys Glu Lys Glu
              355   360   365

Val Glu Ser Leu Lys Leu Pro Ser Glu Lys Asn Ser Asn Lys Ala Lys
       370   375   380

Thr Val Glu Gly Thr Lys Glu Asp Phe Ser Leu Ile Asp Ser Asp Val
385   390   395   400

Asp Gly Leu Thr Asp Ile Thr Val Ser Ser Val His Thr Ser Asp Leu
              405   410   415

Ser Ser Phe Glu Glu Asp Thr Glu Glu Glu Val Val Thr Ser Asp Ser
              420   425   430

Met Glu Glu Gly Glu Ile Thr Ser Asp Asp Glu Glu Lys Asn Lys Gln
              435   440   445

Asn Lys Thr Lys Thr Gln Thr Ser Asp Ser Ser Glu Gly Lys Thr Lys
       450   455   460

Ser Val Arg His Ala Tyr Val His Lys Pro Tyr Leu Tyr Ser Lys Tyr
465   470   475   480

Tyr Ser Asp Ser Asp Asp Glu Leu Thr Val Glu Gln Arg Arg Gln Ser
              485   490   495

Ile Gly Ile Leu Trp Phe
          500

<210> 3009
<211> 61
<212> PRT
<213> Homo sapiens

<400> 3009

Met Lys Arg Phe Leu Phe Leu Leu Leu Thr Ile Ser Leu Leu Val Met
1   5   10   15

Val Gln Ile Gln Thr Gly Leu Ser Gly Gln Asn Asp Thr Ser Gln Thr
              20   25   30

Ser Ser Pro Ser Ala Ser Ser Ser Met Ser Gly Gly Ile Phe Leu Phe
          35   40   45

Phe Val Ala Asn Ala Ile Ile His Leu Phe Cys Phe Ser
      50   55   60

<210> 3010
<211> 352
<212> PRT
<213> Homo sapiens

<400> 3010

Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met
1   5   10   15

Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg Glu Glu
              20   25   30

Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr Ser Ile Ile
          35   40   45

Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly
      50   55   60

Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu
65   70   75   80

Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val
              85   90   95

```
Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu Cys Lys Ala Val
        100                 105                 110

His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala
        115                 120                 125

Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser
    130                 135                 140

Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val Tyr Val Gly Val
145                 150                 155                 160

Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn
            165                 170                 175

Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn
        180                 185                 190

Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu
        195                 200                 205

Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser
        210                 215                 220

Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
225                 230                 235                 240

Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr
            245                 250                 255

Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile Lys Gln
            260                 265                 270

Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser Ile Thr Glu
        275                 280                 285

Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe
        290                 295                 300

Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala Leu Thr Ser Val
305                 310                 315                 320

Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly
            325                 330                 335
```

His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser Phe His Ser Ser
            340   345   350

<210>   3011
<211>   94
<212>   PRT
<213>   Homo sapiens

<400>   3011

Met Ala Pro Leu Lys Met Leu Ala Leu Val Thr Leu Leu Leu Gly Ala
1   5   10   15

Ser Leu Gln His Ile His Ala Ala Arg Gly Thr Asn Val Gly Arg Glu
            20   25   ,   30

Cys Cys Leu Glu Tyr Phe Lys Gly Ala Ile Pro Leu Arg Lys Leu Lys
            35   40   45

Thr Trp Tyr Gln Thr Ser Glu Asp Cys Ser Arg Asp Ala Ile Val Phe
    50   55   60

Val Thr Val Gln Gly Arg Ala Ile Cys Ser Asp Pro Asn Asn Lys Arg
65   70   75   80

Val Lys Asn Ala Val Lys Tyr Leu Gln Ser Leu Glu Arg Ser
            85   90

<210>   3012
<211>   748
<212>   PRT
<213>   Homo sapiens

<400>   3012

Met Ser Gln Trp Asn Gln Val Gln Gln Leu Glu Ile Lys Phe Leu Glu
1   5   10   15

Gln Val Asp Gln Phe Tyr Asp Asp Asn Phe Pro Met Glu Ile Arg His
            20   25   30

Leu Leu Ala Gln Trp Ile Glu Asn Gln Asp Trp Glu Ala Ala Ser Asn
            35   40   45

Asn Glu Thr Met Ala Thr Ile Leu Leu Gln Asn Leu Leu Ile Gln Leu
    50   55   60

Asp Glu Gln Leu Gly Arg Val Ser Lys Glu Lys Asn Leu Leu Leu Ile
65   70   75   80

```
His Asn Leu Lys Arg Ile Arg Lys Val Leu Gln Gly Lys Phe His Gly
              85                  90              95

Asn Pro Met His Val Ala Val Val Ile Ser Asn Cys Leu Arg Glu Glu
             100                 105             110

Arg Arg Ile Leu Ala Ala Ala Asn Met Pro Val Gln Gly Pro Leu Glu
             115                 120             125

Lys Ser Leu Gln Ser Ser Ser Val Ser Glu Arg Gln Arg Asn Val Glu
     130             135             140

His Lys Val Ala Ala Ile Lys Asn Ser Val Gln Met Thr Glu Gln Asp
145                 150             155                 160

Thr Lys Tyr Leu Glu Asp Leu Gln Asp Glu Phe Asp Tyr Arg Tyr Lys
             165                 170             175

Thr Ile Gln Thr Met Asp Gln Ser Asp Lys Asn Ser Ala Met Val Asn
             180                 185             190

Gln Glu Val Leu Thr Leu Gln Glu Met Leu Asn Ser Leu Asp Phe Lys
             195                 200             205

Arg Lys Glu Ala Leu Ser Lys Met Thr Gln Ile Ile His Glu Thr Asp
     210             215             220

Leu Leu Met Asn Thr Met Leu Ile Glu Glu Leu Gln Asp Trp Lys Arg
225                 230             235                 240

Arg Gln Gln Ile Ala Cys Ile Gly Gly Pro Leu His Asn Gly Leu Asp
             245                 250             255

Gln Leu Gln Asn Cys Phe Thr Leu Leu Ala Glu Ser Leu Phe Gln Leu
             260                 265             270

Arg Arg Gln Leu Glu Lys Leu Glu Glu Gln Ser Thr Lys Met Thr Tyr
             275                 280             285

Glu Gly Asp Pro Ile Pro Met Gln Arg Thr His Met Leu Glu Arg Val
     290             295             300

Thr Phe Leu Ile Tyr Asn Leu Phe Lys Asn Ser Phe Val Val Glu Arg
305                 310             315                 320
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Gln Pro Cys Met Pro Thr His Pro Gln Arg Pro Leu Val Leu Lys Thr
            325   330   335

Leu Ile Gln Phe Thr Val Lys Leu Arg Leu Leu Ile Lys Leu Pro Glu
            340   345   350

Leu Asn Tyr Gln Val Lys Val Lys Ala Ser Ile Asp Lys Asn Val Ser
            355   360   365

Thr Leu Ser Asn Arg Arg Phe Val Leu Cys Gly Thr Asn Val Lys Ala
    370   375   380

Met Ser Ile Glu Glu Ser Ser Asn Gly Ser Leu Ser Val Glu Phe Arg
385   390   395   400

His Leu Gln Pro Lys Glu Met Lys Ser Ser Ala Gly Gly Lys Gly Asn
            405   410   415

Glu Gly Cys His Met Val Thr Glu Glu Leu His Ser Ile Thr Phe Glu
            420   425   430

Thr Gln Ile Cys Leu Tyr Gly Leu Thr Ile Asp Leu Glu Thr Ser Ser
            435   440   445

Leu Pro Val Val Met Ile Ser Asn Val Ser Gln Leu Pro Asn Ala Trp
    450   455   460

Ala Ser Ile Ile Trp Tyr Asn Val Ser Thr Asn Asp Ser Gln Asn Leu
465   470   475   480

Val Phe Phe Asn Asn Pro Pro Pro Ala Thr Leu Ser Gln Leu Leu Glu
            485   490   495

Val Met Ser Trp Gln Phe Ser Ser Tyr Val Gly Arg Gly Leu Asn Ser
            500   505   510

Asp Gln Leu His Met Leu Ala Glu Lys Leu Thr Val Gln Ser Ser Tyr
            515   520   525

Ser Asp Gly His Leu Thr Trp Ala Lys Phe Cys Lys Glu His Leu Pro
    530   535   540

Gly Lys Ser Phe Thr Phe Trp Thr Trp Leu Glu Ala Ile Leu Asp Leu
545   550   555   560

Ile Lys Lys His Ile Leu Pro Leu Trp Ile Asp Gly Tyr Val Met Gly

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            565                    570                    575


Phe Val Ser Lys Glu Lys Glu Arg Leu Leu Leu Lys Asp Lys Met Pro
            580                    585                590


Gly Thr Phe Leu Leu Arg Phe Ser Glu Ser His Leu Gly Gly Ile Thr
            595                600                605


Phe Thr Trp Val Asp His Ser Glu Ser Gly Glu Val Arg Phe His Ser
    610                615                620


Val Glu Pro Tyr Asn Lys Gly Arg Leu Ser Ala Leu Pro Phe Ala Asp
625                630                635                640


Ile Leu Arg Asp Tyr Lys Val Ile Met Ala Glu Asn Ile Pro Glu Asn
                645                650                655


Pro Leu Lys Tyr Leu Tyr Pro Asp Ile Pro Lys Asp Lys Ala Phe Gly
            660                665                670


Lys His Tyr Ser Ser Gln Pro Cys Glu Val Ser Arg Pro Thr Glu Arg
            675                680                685


Gly Asp Lys Gly Tyr Val Pro Ser Val Phe Ile Pro Ile Ser Thr Ile
            690                695                700


Arg Ser Asp Ser Thr Glu Pro His Ser Pro Ser Asp Leu Leu Pro Met
705                710                715                720


Ser Pro Ser Val Tyr Ala Val Leu Arg Glu Asn Leu Ser Pro Thr Thr
            725                730                735


Ile Glu Thr Ala Met Lys Ser Pro Tyr Ser Ala Glu
            740                745
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<210>  3013
<211>  92
<212>  PRT
<213>  Homo sapiens

<400>  3013

Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala
1              5                  10                 15


Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
            20                 25                 30
```

Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
        35   40   45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
    50   55   60

Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65   70   75   80

Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
                85   90

<210>   3014
<211>   444
<212>   PRT
<213>   Homo sapiens

<400>   3014

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln
1   5   10   15

Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val
            20   25   30

Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro
        35   40   45

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu
    50   55   60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile
65   70   75   80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly
            85   90   95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro
            100   105   110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile
        115   120   125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr
    130   135   140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala

145   150   155   160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile
                165   170   175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val
                180   185   190

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu
                195   200   205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile
        210   215   220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg
225   230   235   240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly
                245   250   255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr
                260   265   270

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln
                275   280   285

Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg
        290   295   300

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser
305   310   315   320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met
                325   330   335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser
                340   345   350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala
                355   360   365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly
        370   375   380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val
385   390   395   400

1450

```
Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr
            405                     410                 415


Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu
            420                 425                 430


Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro
        435                 440
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<210>  3015
<211>  769
<212>  PRT
<213>  Homo sapiens

<400>  3015
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Met Leu Gly Leu Arg Pro Pro Leu Leu Ala Leu Val Gly Leu Leu Ser
1               5                   10                  15


Leu Gly Cys Val Leu Ser Gln Glu Cys Thr Lys Phe Lys Val Ser Ser
            20                  25                  30


Cys Arg Glu Cys Ile Glu Ser Gly Pro Gly Cys Thr Trp Cys Gln Lys
            35                  40                  45


Leu Asn Phe Thr Gly Pro Gly Asp Pro Asp Ser Ile Arg Cys Asp Thr
    50                  55                  60


Arg Pro Gln Leu Leu Met Arg Gly Cys Ala Ala Asp Asp Ile Met Asp
65                  70                  75                  80


Pro Thr Ser Leu Ala Glu Thr Gln Glu Asp His Asn Gly Gly Gln Lys
                85                  90                  95


Gln Leu Ser Pro Gln Lys Val Thr Leu Tyr Leu Arg Pro Gly Gln Ala
            100                 105                 110


Ala Ala Phe Asn Val Thr Phe Arg Arg Ala Lys Gly Tyr Pro Ile Asp
            115                 120                 125


Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Leu Asp Asp Leu Arg
    130                 135                 140


Asn Val Lys Lys Leu Gly Gly Asp Leu Leu Arg Ala Leu Asn Glu Ile
145                 150                 155                 160
```

Thr Glu Ser Gly Arg Ile Gly Phe Gly Ser Phe Val Asp Lys Thr Val
              165   170   175

Leu Pro Phe Val Asn Thr His Pro Asp Lys Leu Arg Asn Pro Cys Pro
              180   185   190

Asn Lys Glu Lys Glu Cys Gln Pro Pro Phe Ala Phe Arg His Val Leu
              195   200   205

Lys Leu Thr Asn Asn Ser Asn Gln Phe Gln Thr Glu Val Gly Lys Gln
    210   215   220

Leu Ile Ser Gly Asn Leu Asp Ala Pro Glu Gly Gly Leu Asp Ala Met
225   230   235   240

Met Gln Val Ala Ala Cys Pro Glu Glu Ile Gly Trp Arg Asn Val Thr
              245   250   255

Arg Leu Leu Val Phe Ala Thr Asp Asp Gly Phe His Phe Ala Gly Asp
              260   265   270

Gly Lys Leu Gly Ala Ile Leu Thr Pro Asn Asp Gly Arg Cys His Leu
              275   280   285

Glu Asp Asn Leu Tyr Lys Arg Ser Asn Glu Phe Asp Tyr Pro Ser Val
    290   295   300

Gly Gln Leu Ala His Lys Leu Ala Glu Asn Asn Ile Gln Pro Ile Phe
305   310   315   320

Ala Val Thr Ser Arg Met Val Lys Thr Tyr Glu Lys Leu Thr Glu Ile
              325   330   335

Ile Pro Lys Ser Ala Val Gly Glu Leu Ser Glu Asp Ser Ser Asn Val
              340   345   350

Val His Leu Ile Lys Asn Ala Tyr Asn Lys Leu Ser Ser Arg Val Phe
    355   360   365

Leu Asp His Asn Ala Leu Pro Asp Thr Leu Lys Val Thr Tyr Asp Ser
    370   375   380

Phe Cys Ser Asn Gly Val Thr His Arg Asn Gln Pro Arg Gly Asp Cys
385   390   395   400

Asp Gly Val Gln Ile Asn Val Pro Ile Thr Phe Gln Val Lys Val Thr

                    405   410   415

Ala Thr Glu Cys Ile Gln Glu Gln Ser Phe Val Ile Arg Ala Leu Gly
            420   425   430

Phe Thr Asp Ile Val Thr Val Gln Val Leu Pro Gln Cys Glu Cys Arg
            435   440   445

Cys Arg Asp Gln Ser Arg Asp Arg Ser Leu Cys His Gly Lys Gly Phe
    450   455   460

Leu Glu Cys Gly Ile Cys Arg Cys Asp Thr Gly Tyr Ile Gly Lys Asn
465   470   475   480

Cys Glu Cys Gln Thr Gln Gly Arg Ser Ser Gln Glu Leu Glu Gly Ser
                485   490   495

Cys Arg Lys Asp Asn Asn Ser Ile Ile Cys Ser Gly Leu Gly Asp Cys
            500   505   510

Val Cys Gly Gln Cys Leu Cys His Thr Ser Asp Val Pro Gly Lys Leu
            515   520   525

Ile Tyr Gly Gln Tyr Cys Glu Cys Asp Thr Ile Asn Cys Glu Arg Tyr
    530   535   540

Asn Gly Gln Val Cys Gly Gly Pro Gly Arg Gly Leu Cys Phe Cys Gly
545   550   555   560

Lys Cys Arg Cys His Pro Gly Phe Glu Gly Ser Ala Cys Gln Cys Glu
            565   570   575

Arg Thr Thr Glu Gly Cys Leu Asn Pro Arg Arg Val Glu Cys Ser Gly
            580   585   · 590

Arg Gly Arg Cys Arg Cys Asn Val Cys Glu Cys His Ser Gly Tyr Gln
            595   600   605

Leu Pro Leu Cys Gln Glu Cys Pro Gly Cys Pro Ser Pro Cys Gly Lys
    610   615   620

Tyr Ile Ser Cys Ala Glu Cys Leu Lys Phe Glu Lys Gly Pro Phe Gly
625   630   635   640

Lys Asn Cys Ser Ala Ala Cys Pro Gly Leu Gln Leu Ser Asn Asn Pro
                645   650   655

```
Val Lys Gly Arg Thr Cys Lys Glu Arg Asp Ser Glu Gly Cys Trp Val
         660                 665             670

Ala Tyr Thr Leu Glu Gln Gln Asp Gly Met Asp Arg Tyr Leu Ile Tyr
         675                 680             685

Val Asp Glu Ser Arg Glu Cys Val Ala Gly Pro Asn Ile Ala Ala Ile
         690                 695             700

Val Gly Gly Thr Val Ala Gly Ile Val Leu Ile Gly Ile Leu Leu Leu
705             710                 715                 720

Val Ile Trp Lys Ala Leu Ile His Leu Ser Asp Leu Arg Glu Tyr Arg
             725                 730                 735

Arg Phe Glu Lys Glu Lys Leu Lys Ser Gln Trp Asn Asn Asp Asn Pro
         740                 745                 750

Leu Phe Lys Ser Ala Thr Thr Thr Val Met Asn Pro Lys Phe Ala Glu
         755                 760                 765

Ser
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<210>  3016
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<212>  DNA
<213>  Homo sapiens

<400>  3016
gggaggaaca ctgcactctt aagcttccgc cgtctcaacc cctcacagga                    50


<210>  3017
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3017
aggagtcttt tacccggtgt gctttgccgc agtcatccaa aataaattca                    50


<210>  3018
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3018
cacctgattc cccctcttgc ccacaggact ctgctgttgt tttcattctg                    50
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<210>  3019
<211>  50
<212>  DNA
<213>  Homo sapiens

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<210>  3020
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<212>  DNA
<213>  Homo sapiens

<400>  3020
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<210>  3021
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<212>  DNA
<213>  Homo sapiens

<400>  3021
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<210>  3022
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<212>  DNA
<213>  Homo sapiens

<400>  3022
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<210>  3023
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3023
taagcataaa acctgacacg ttaaaatccc tgccctttgg tgagcccact                    50


<210>  3024
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<212>  DNA
<213>  Homo sapiens

<400>  3024
tgctggtatt ctcactgcca catttttgga aacctgtatt acaccttaaa                    50


<210>  3025
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3025
cagtcactgg gtctatatta aacagcaacc agagcaacaa atggcaaaca                    50
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<210> 3026
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3026
tctagcccag cattgatcta gaagcagagg aatcccagcg ccttttaaaa   50

<210> 3027
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<212> DNA
<213> Homo sapiens

<400> 3027
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<210> 3028
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3028
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<210> 3029
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<212> DNA
<213> Homo sapiens

<400> 3029
ggtctgagag tctgtgaaga tggcccagtc ttctatcccc cacctaaaaa   50

<210> 3030
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<212> DNA
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cttgaccaaa cccacagcct gtctcttctc ttgtttagtt acttacggca   50

<210> 3031
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<212> DNA
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<400> 3031
ccactgtcac tgtttctctg ctgttgcaaa tacatggata acacatttga   50

<210> 3032
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<212> DNA
<213> Homo sapiens

<400> 3032
tgcagccact attgttagtc tcttgattca taatgactta agcacacttg   50

<210> 3033
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<212> DNA
<213> Homo sapiens

<400> 3033
cctgatggag agaagaaggc atatgttcga ctggctcctg attacgatgc   50

<210> 3034
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<212> DNA
<213> Homo sapiens

<400> 3034
gccgaattgt ctttggtgct tttcacttgt gttttaaaat aaggattttt   50

<210> 3035
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<212> DNA
<213> Homo sapiens

<400> 3035
ctggaggacc tgttgatgct agttcagagt atcaccaaga gctggagagg   50

<210> 3036
<211> 50
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<400> 3036
accatccaat cggacaagct ttcagaacct tattgaagga tttgaagcac   50

<210> 3037
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<212> DNA
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<400> 3037
agaaatgttc agtaatgaaa aaatatatcc aatcagagcc atcccgaaaa   50

<210> 3038
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<212> DNA
<213> Homo sapiens

<400> 3038
agcggactca ggctccagct gtggctacaa cataggggttt ttatacaaga   50

<210> 3039
<211> 50
<212> DNA

<213> Homo sapiens

<400> 3039
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<210> 3040
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3040
ccactgtcac tgtttctctg ctgttgcaaa tacatggata acacatttga   50

<210> 3041
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3041
aagtgaacaa aataagcaac taaatgagac ctaataattg gccttcgatt   50

<210> 3042
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<212> DNA
<213> Homo sapiens

<400> 3042
tctgttgata gctggagaac tttagtttca agtactacat tgtgaaagca   50

<210> 3043
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<212> DNA
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<400> 3043
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<210> 3044
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ctgaccgcca ctctcacatt tgggctcttc gctggccttg gtggagctgg   50

<210> 3045
<211> 50
<212> DNA
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<210> 3046

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<212>  DNA
<213>  Homo sapiens

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<210>  3047
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<213>  Homo sapiens

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agaggactat agtggaagtg aaagcattct gtgtttactc tttgcattaa              50


<210>  3048
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<213>  Homo sapiens

<400>  3048
caggtcaacc cccaccggac ctacaacccg cagtcccaca tcatctcagg              50


<210>  3049
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ccttccagaa gctacgaaaa agggagctgt ttaaatttaa taaatctctg              50


<210>  3050
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<210>  3051
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atctgacatt attgtaacta ccgtgtgatc agtaagattc ctgtaagaaa              50


<210>  3052
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tccaatgcag tcccattctt tatggcctat agtctcactc ccaactaccc              50
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tcctaggtag ggtttaatcc ccagtaaaat tgccatattg cacatgtctt          50


<210>  3054
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<210>  3055
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aaagggtttt atccactgtc atttcaattg gataacattt tgtcaagttt          50


<210>  3056
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<212>  DNA
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<400>  3056
aattcctgaa ccgttggatc accttctgtc agtccatcat ctccaccctg          50


<210>  3057
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<400>  3057
ggcaggaggt tctcactgtt gtgaaggttg tagacgttgt gtaatgtgtt          50


<210>  3058
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3058
gtgggtaagg ggctcaagct gtgatgctgc tggttttatc tctagtgaaa          50


<210>  3059
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<212>  DNA
<213>  Homo sapiens

<400>  3059
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agacaaagag agcataaata tagctctact catgggtacc ataccagtgt   50

<210> 3060
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<212> DNA
<213> Homo sapiens

<400> 3060
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<210> 3061
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3061
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<210> 3062
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3062
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<210> 3063
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3063
tgatctgact ggaaaacaat cctgtatccc ctcccaaaga atcatgggct   50

<210> 3064
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<212> DNA
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<400> 3064
aacaagccat gtttgcccta gtccaggatt gcctcacttg agacttgcta   50

<210> 3065
<211> 50
<212> DNA
<213> Homo sapiens

<400> 3065
acagcatgag aaactgttag tacgcatacc tcagttcaaa cctttaggga   50

<210> 3066
<211> 50
<212> DNA
<213> Homo sapiens

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<210>  3067
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<212>  DNA
<213>  Homo sapiens

<400>  3067
gagagctttc tccccgcctt cagtttctga tggatctagc catgttgaaa                50


<210>  3068
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<212>  DNA
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ggaggaatgg ctgtgcccgt cccctccact taagcgacct gagtctccag                50


<210>  3069
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<213>  Homo sapiens

<400>  3069
ggaaatgttg ctgtggggga ttcattgtaa ctctccttgt gaactgctca                50


<210>  3070
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<212>  DNA
<213>  Homo sapiens

<400>  3070
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<210>  3071
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<212>  DNA
<213>  Homo sapiens

<400>  3071
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<210>  3072
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<400>  3072
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<210>  3073
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<212>  DNA
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<210>  3074
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<212>  DNA
<213>  Homo sapiens

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tgtgctaagc ctgatgaaat gtgctccttc aatctccatg aaaccatcgt          50


<210>  3075
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<212>  DNA
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<210>  3076
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<212>  DNA
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<400>  3076
ataacagact ccagctcctg gtccacccgg catgtcagtc agcactctgg          50


<210>  3077
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<210>  3078
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<210>  3079
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<212>  DNA
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<212>  DNA
<213>  Homo sapiens

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<210>  3081
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<212>  DNA
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aattttaagt gtccgaataa gatatgtctt ttttgtttgt ttttttttggt tggttgtttg    4920

tttttatca tctgagattc tgtaatgtat ttgcaaataa tggatcaatt aatttttttt    4980

gaagctcata ttgtatcttt ttaaaaacca tgttgtggaa aaaagccaga gtgacaagtg    5040

acaaaatcta tttaggaact ctgtgtatga atcctgattt taactgctag gattcagcta    5100

aatttctgag ctttatgatc tgtggaaatt tggaatgaaa tcgaattcat tttgtacata    5160

catagtatat taaaactata taatagttca tagaaatgtt cagtaatgaa aaaatatatc    5220

caatcagagc catcccgaaa aaaaaaaaa aa                                     5252
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<210> 3103
<211> 841
<212> DNA
<213> Homo sapiens

<400> 3103
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agagaaggaa tattgggtta caatctgaat ttctctttat gatttctctt aaagtataga        180

acagctatta aaatgactaa tattgctaaa atgaaggcta ctaaatttcc ccaagaattt        240

cggtggaatg cccaaaaatg gtgttaagat atgcagaagg gcccatttca agcaaagcaa        300

tctctccacc ccttcataaa agatttaagc taaaaaaaaa aaaaaaagaa gaaaatccaa        360

cagctgaaga cattgggcta tttataaatc ttctcccagt cccccagaca gcctcacatg        420

ggggctgtaa acagctaact aaaatatctt tgagactctt atgtccacac ccactgacac        480

aaggagagct gtaaccacag tgaaactaga ctttgctttc ctttagcaag tatgtgccta        540

tgatagtaaa ctggagtaaa tgtaacagta ataaacaaa ttttttttaa aaataaaaat        600

tatacctttt tctccaacaa acggtaaaga ccacgtgaag acatccataa aattaggcaa        660

ccagtaaaga tgtggagaac cagtaaactg tcgaaattca tcacattatt ttcatacttt       ·720

aatacagcag ctttaattat tggagaacat caaagtaatt aggtgccgaa aaacattgtt        780

attaatgaag ggaacccctg acgtttgacc ttttctgtac catctatagc cctggacttg        840

a                                                                         841
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<211>   841
<212>   DNA
<213>   Homo sapiens


<220>
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<222>   (94)..(121)
<223>   n is a, c, g, t or u

<220>
<221>   misc_feature
<222>   (569)..(604)
<223>   n is a, c, g, t or u

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aagtgttcct ctaaattaga aaggcatcac tacnnnnnnn nnnnnnnnnn nnnnnnnnnn        120

ngagaaggaa tattgggtta caatctgaat ttctctttat gatttctctt aaagtataga        180

acagctatta aaatgactaa tattgctaaa atgaaggcta ctaaatttcc ccaagaattt        240

cggtggaatg cccaaaaatg gtgttaagat atgcagaagg gcccatttca agcaaagcaa        300

tctctccacc ccttcataaa agatttaagc taaaaaaaaa aaaaaaagaa gaaaatccaa        360

cagctgaaga cattgggcta tttataaatc ttctcccagt cccccagaca gcctcacatg        420
```

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ggggctgtaa acagctaact aaaatatctt tgagactctt atgtccacac ccactgacac    480

aaggagagct gtaaccacag tgaaactaga ctttgctttc ctttagcaag tatgtgccta    540

tgatagtaaa ctggagtaaa tgtaacagnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn    600

nnnnccttt tctccaacaa acggtaaaga ccacgtgaag acatccataa aattaggcaa    660

ccagtaaaga tgtggagaac cagtaaactg tcgaaattca tcacattatt ttcatacttt    720

aatacagcag ctttaattat tggagaacat caaagtaatt aggtgccgaa aaacattgtt    780

attaatgaag ggaacccctg acgtttgacc ttttctgtac catctatagc cctggacttg    840

a                                                                    841
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<210>  3105
<211>  63
<212>  DNA
<213>  Homo sapiens

<400>  3105
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ttt                                                                  63
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<210>  3106
<211>  609
<212>  DNA
<213>  Homo sapiens

<220>
<221>  misc_feature
<222>  (303)..(304)
<223>  n is a, c, g, t or u

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catgaccttg actgatgcag gtgtctaggg atacaggtca cacagccgtc catccccgtc    120

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accatgacga gagcttggca gaataaataa cttctttaaa caattttacg gcatgaagaa    240

atctggacca gtttattaaa tgggatttct gccacaaacc ttggaagaat cacatcatct    300

tanncccaag tgaaaactgt gttgcgtaac aaagaacatg actgcgctcc acacatacat    360

cattgcccgg cgaggcggga cacaagtcaa cgacggaaca cttgagacag gcctacaact    420

gtgcacgggt cagaagcaag tttaagccat acttgctgca gtgagactac atttctgtct    480

atagaagata cctgacttga tctgtttttc agctccagtt cccagatgtg cgtgttgtgg    540

tccccaagta tcaccttcca atttctggga gcagtgctct ggccggatcc ttgccgcgcg    600

gataaaaac                                                            609
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<210>  3107
<211>  50
<212>  DNA
<213>  Homo sapiens

<400>  3107
gaaattggaa ggtgatactt ggggaccaca acacgcacat ctgggaactg              50


<210>  3108
<211>  738
<212>  DNA
<213>  Homo sapiens

<400>  3108
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tcttcacctt catctcttcc tcgggatgtc tgtcagggtt caccttggca tcaatttgcc    180

ctgaaactta gctgtgctgg gattattctc cttgtcttgg ttgttactgg gttgagtgtt    240

tcagtgacat ccttaataca gaaatcatca atagaaaaat gcagtgtgga cattcaacag    300

agcaggaata aaacaacaga gagaccgggt ctcttaaact gcccaatata ttggcagcaa    360

ctccgagaga aatgcttgtt attttctcac actgtcaacc cttggaataa cagtctagct    420

gattgttcca ccaaagaatc cagcctgctg cttattcgag ataaggatga attgatacac    480

acacagaacc tgatacgtga caaagcaatt ctgttttgga ttggattaaa tttttcatta    540

tcagaaaaga actggaagtg gataaacggc tcttttttaa attctaatga cttagaaatt    600

agaggtgatg ctaaagaaaa cagctgtatt tccatctcac agacatctgt gtattctgag    660

tactgtagta cagaaatcag atggatctgc caaaaagaac taacacctgt gagaaataaa    720

gtgtatcctg actcttga                                                  738


<210>  3109
<211>  3809
<212>  DNA
<213>  Homo sapiens

<400>  3109
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gcgcaggcgg ccgtggggcc cggagggcgc gcccggcccg aggtgcgctc gatggtggac    180

gtgctggcgg accacgcagg cgagctcgtg cgcaccgaca gcccaacttc cctctgctcc    240

gtgctgccct cgcactggcg ctgcaacaag acgctgcccg tcgccttcaa ggtggtggca    300

ttgggggacg tgccggatgg tacggtggtg actgtgatgg caggcaatga cgagaactac    360
```

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tccgctgagc tgcgcaatgc ctcggccgtc atgaagaacc aggtggccag gttcaacgac    420

cttcgcttcg tgggccgcag tgggcgaggg aagagtttca ccctgaccat cactgtgttc    480

accaacccca cccaagtggc gacctaccac cgagccatca aggtgaccgt ggacggaccc    540

cgggagccca gacggcaccg gcagaagctg gaggaccaga ccaagccgtt ccctgaccgc    600

tttggggacc tggaacggct gcgcatgcgg gtgacaccga gcacacccag cccccgaggc    660

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aaccagagcg ggcccttcca ggccaacccg tcccccctacc acctctacta cgggacatcc   1020

tctggctcct accagttctc catggtggcc ggcagcagca gtgggggcga ccgctcacct   1080

acccgcatgc tggcctcttg caccagcagc gctgcctctg tcgccgccgg caacctcatg   1140

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ttccagagag aggcagcatt ggcccacagg ataagcctca ggccctggga aacctcccga   1680

cccctgcacc ttcgttggag ccctgcatc ccctgggtcc agcccctct gcatttacac   1740

agatttgagt cagaactgga aagtgtcccc caccccacc accctcgagc ggggttcccc   1800

tcattgtaca gatggggcag gacccagcac gctgctggca gagatggttt gagaacacat   1860

ccaagccagt ccccccagcc cagcttcccc tccgttccta actgttggct ttcccccagc   1920

cgcacggtcc caggcccaga gaagatgagt ctatggcatc aggttcttaa accaggaaag   1980

cacctacaga ccggctcctc catgcacttt accagctcaa cgcatccact ctctgttctc   2040

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catttgtgga gagaacagga gggccagata gataggtcct agcagaaggc attgaggtga   2160
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gggatcattt tgggtcagac atcaatgtcc ctgtcccccc tgggtccagc caagctgtgc   2220

cccatccccc aagcctcctg ggaggatcca gccaaatctt gcgactcctg gcacacacct   2280

gtctgtaacc tgttttgtgc tctgaaagca aatagtcctg agcaaaaaaa aaaaaaaaaa   2340

acaaaaaaac aaaaaaaaaa caaaacagtt tttaaaactg attttagaaa aagaagctta   2400

atctaacgtt ttcaaacaca aggtctctta caggtatagt tccgtgatta tgatagctct   2460

gtgattataa gcaacatccc cgccccctct ccccccgcg daccccagc tgcctcctga   2520

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aaatgggaaa gtgggcgctt gccaagggcc aggctgcatg gattctcaca tcagagttct   2880

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tattttaact ttctgcctcg gcctctgtgg atgcagaaat ctgccctaca aaatgctctt   3000

cattggttgt ctctgtgaga gcactgtccc cacccaacct gtcacaacgg ccagaaccat   3060

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ccttcctgat cctggagagg cagggatagt aaataaattg ctcttcctac cccatccccc   3420

atcccctgac aaaaagtgac ggcagccgta ctgagtctgt aaggcccaaa gtgggtacag   3480

acagcctggg ctggtaaaag taggtcctta tttacaaggc tgcgttaaag ttgtactagg   3540

caaacacact gatgtaggaa gcacgaggaa aggaagacgt tttgatatag tgttactgtg   3600

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aactgctttg cactatcgtt tgcttggtgt ttgtttttaa cgcacaactt gcttgtacag   3780

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<212>   DNA
<213>   Homo sapiens

<400> 3110

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tactctggat caagtgtggc ccagaaggtt actcaagccc agtcatcagt atccatgcca     120

gtgaggaaag cagtcaccct gaactgcctg tatgaaacaa gttggtggtc atattatatt     180

ttttggtaca agcaacttcc cagcaaagag atgattttcc ttattcgcca gggttctgat     240

gaacagaatg caaaaagtgg tcgctattct gtcaacttca agaaagcagc gaaatccgtc     300

gccttaacca tttcagcctt acagctagaa gattcagcaa agtacttttg tgctcttggg     360

acgggggtga ggggactcca ggacaccgat aaactcatct ttggaaaagg aacccgtgtg     420

actgtggaac caagaagtca gcctcatacc aaaccatccg tttttgtcat gaaaaatgga     480

acaaatgtcg cttgtctggt gaaggaattc taccccaagg atataagaat aaatctcgtg     540

tcatccaaga agataacaga gtttgatcct gctattgtca tctctcccag tgggaagtac     600

aatgctgtca agcttggtaa atatgaagat tcaaattcag tgacatgttc agttcaacac     660

gacaataaaa ctgtgcactc cactgacttt gaagtgaaga cagattctac agatcacgta     720

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tgactggcat gaggaagcta cactcctgaa gaaaccaaag gcttacaaaa atgcatctcc     960

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agacaaaagt cctggggaag gggggtttat gtcctaactg ctttgtatgc tgttttataa    1140

agggatagaa ggatataaaa a                                              1161
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<210> 3111
<211> 611
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (543)..(543)
<223> n is a, c, g, t or u

<400> 3111

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tataagttac atattttaag aaaaatcagt cattttttcat atataattgc aaagaattaa     120

gatcatttaa ctttagcact ataagcaagc attaaattaa atgcactcag attttttggca     180
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cattatatgg cattccttat accacatatt tataagatct aaaggattat aaacatatta      240

cacataataa ttaagtccaa tataaattgt gttcaggtta taaaatgccc tatttaagtt      300

gtgctcttgg tgagggtgaa cagaaaagaa aaggcttctt ctttagccct taagcctatg      360

acacaatttc catgctggta attcctttca tcttctgaag aatctctatt ttattataac      420

attattggct ttcagcttgg aatttctcta cgcagattgt ctattgacag tgccaaggaa      480

acatctcact gtccacagaa tagcagcctc cacccagttg aaagctgcac attgtttcca      540

ctntaccatt ggtacttccc tctgatggca tccagcacac gaccattagc ctgagtgatg      600

cccaactgag c                                                           611
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<210>  3112
<211>  572
<212>  DNA
<213>  Homo sapiens

<400>  3112
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gaggcctagc aagtctcaag tgaggcaatc ctggactagg gcaaacatgg cttgttccaa      120

aagccggggg ttaaggaatc aaagtcaggt gaaactatca ctttcacaaa agctttcctt      180

gactcctggg cctagtatct tttgcccctg gcagaatgta acagcaaaat gtctccttct      240

gaaacggaag gcacagccct ctttcagaag caaaacacct taacactcgg cttctatttg      300

cttaagaatt tacaaataga aatgagaatc aaaggtttta actcatctga tagcactggg      360

cacccaatgt tcacagcctg cttctttgaa ttgttagtgt ctccccaata aataaataca      420

gaaccttgga tacccttcga attttaaaat accttaaagt cttccattaa tcttattttt      480

taaaaatgct aggtttgttt cagttacctg cagcaatcaa aaagctttgg caccttcttt      540

tagagaattg cacaaaacag gatgcatcaa gg                                    572
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<210>  3113
<211>  1026
<212>  DNA
<213>  Homo sapiens

<400>  3113
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tctgggctcc aggcagaagc acagcctccc cgacctgccc tacgactacg gcgccctgga      120

acctcacatc aacgcgcaga tcatgcagct gcaccacagc aagcaccacg cggcctacgt      180

gaacaacctg aacgtcaccg aggagaagta ccaggaggcg ttggccaagg gagatgttac      240

agcccagata gctcttcagc ctgcactgaa gttcaatggt ggtggtcata tcaatcatag      300

cattttctgg acaaacctca gccctaacgg tggtggagaa cccaaagggg agttgctgga      360
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agccatcaaa ctggactttg gttcctttga caagtttaag gagaagctga cggctgcatc   420

tgttggtgtc caaggctcag gttggggttg gcttggtttc aataaggaac ggggacactt   480

acaaattgct gcttgtccaa atcaggatcc actgcaagga acaacaggcc ttattccact   540

gctggggatt gatgtgtggg agcacgctta ctaccttcag tataaaaatg tcaggcctga   600

ttatctaaaa gctatttgga atgtaatcaa ctgggagaat gtaactgaaa gatacatggc   660

ttgcaaaaag taaaccacga tcgttatgct gagtatgtta agctctttat gactgttttt   720

gtagtggtat agagtactgc agaatacagt aagctgctct attgtagcat ttcttgatgt   780

tgcttagtca cttatttcat aaacaactta atgttctgaa taatttctta ctaaacattt   840

tgttattggg caagtgattg aaaatagtaa atgctttgtg tgattgaatc tgattggaca   900

ttttcttcag agagctaaat tacaattgtc atttataaaa ccatcaaaaa tattccatcc   960

atatactttg gggacttgta gggatgcctt tctagtccta ttctattgca gttatagaaa   1020

atctag   1026

<210> 3114
<211> 1271
<212> DNA
<213> Homo sapiens

<400> 3114
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tataatacat gtctcaccaa tagatgattc aagaacatca tttaaataca caatttttca   120

ttctctattt ttgctaaatt tcttcatact caactttcag attctttaat ctccagctca   180

gcttcaacaa ttcaacgctg ttctttctga aaaagtacac atcgtgcctt ctctacttcg   240

ctcttggaac ataatttctc atggcagctt ttactaaact gagtattgag ccagcattta   300

ctccaggacc aacatagaa ctccagaaag actctgactg ctgttcttgc caagaaaaat   360

gggttgggta ccggtgcaac tgttacttca tttccagtga acagaaaact tggaacgaaa   420

gtcggcatct ctgtgcttct cagaaatcca gcctgcttca gcttcaaaac acagatgaac   480

tggattttat gagctccagt caacaatttt actggattgg actctcttac agtgaggagc   540

acaccgcctg gttgtgggag aatggctctg cactctccca gtatctattt ccatcatttg   600

aaacttttaa tacaaagaac tgcatagcgt ataatccaaa tggaaatgct ttagatgaat   660

cctgtgaaga taaaaatcgt tatatctgta agcaacagct catttaaatg tttcttgggg   720

cagagaaggt ggagagtaaa gacccaacat tactaacaat gatacagttg catgttatat   780

tattactaat tgtctacttc tggagtctat aaaatgtttt taaacagtgt catatacaat   840

tgtcatgtat gtgaaacaat gtgtttttaaa attgatgaaa ttcgttcacc tacatttgag   900

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aattataaaa ttaacataaa gaattttgta ttttcattta atgtatataa tgttaaattc        960

aatgtagttt tattacacat ttatgtaatt ttatttacat tcttgctaat tctcagcaga       1020

aatttaaata agatttaatt cacatcaaat aaaatttaga aaataaaatt taactcacac       1080

tgcccaggct ggagcatagt ggcaagatca tagctcattg caagctcaag tgatcctcct       1140

gactcagcct cccaagtagc taggactgca ggcaccatgt cactatgccc gactaatttt       1200

taattttaa ttttttgtca agacaaggtc ttgctatgtt gcccaggctg gtcttgaact       1260

cctggcctca a                                                            1271
```

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<210> 3115
<211> 358
<212> DNA
<213> Homo sapiens

<400> 3115
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atgaacaagt aaaaacacac acagcaaaat ttacatcaaa attattacgt ggtacagaat        120

ccaaaagtca taaaaagcaa aagctatctt tttttcactc tggcacccat ctgttcttcc        180

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caagcacaga cttatattga ttctaaaaga ataagagaca ttttcagcat gttgctttgt        300

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tgcccctggc tacctcttgg gcatctgcag cggtgaatgg cacttcccag ttcacatgct        240

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